

Excerpts from

The NEURONS and NEURAL SYSTEM: a 21st CENTURY PARADIGM

This material is excerpted from the full β -version of the text. The final printed version will be more concise due to further editing and economical constraints.

A Table of Contents and an index are located at the end of this paper.

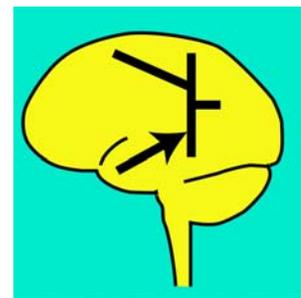
A few cross ref's have yet to be defined and are indicated by "XXX."

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Neural Concepts

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[xxx incorporate material from Rolls, E. & Deco, G. (2002) Computational Neuroscience of Vision. NY: Oxford Univ Press as presented in Chapter 4 in this chapter.]
[xxx look at Friston work on brain mapping (references in Friston

12 Stage 5, Cognition, Information Manipulation Within the Pre-Frontal Lobe and its Engines ¹

12.1 Introduction

This chapter will be more conceptual than the earlier chapters because it is approaching the leading edge of neurobiology and neuropsychology. It is forced to review large volumes of less than precise information about a very complex structure dealing with non-sensorytopic "information" extracted from sensorytopic representations. At the leading edge of neuroscience, the chiasm between neuroscience and philosophy is quite apparent. Philosophy has attempted to offer models related to cognition but they remain in the realm of symbolic logic and based largely on introspection first and observation of others second.

Van Gelder provided a sweeping discussion of potential cognitive operations in 1995 but he did not provided any detailed framework or even block diagrams². He has, however, asserted the likelihood that cognition is achieved through "image matching" rather than bulk computation as in a typical digital computer. This image matching is envisioned as occurring largely in an analog domain (using the Watt governor as a simplified analog). He describes non-computational machines operating in the analog domain as dynamical systems (page 367) and based on a linear differential equation. Such a system employs continuous, rather than quantized, values for the variables. He notes the conventional computational approach has lost most of its luster from the 1980's. Haikonen has recently reiterated the concept of associative processing as a potential basis for cognition³.

Baars & Gage published a textbook on Cognition, Brain & Consciousness in 2007⁴. It is largely an introductory text relying more on pictures than detailed discussion and not providing citations to many of the assertions put forward.

Baars & Gage made an astounding statement on page 60, "The great diversity of the neurons in the brain is suggested by Figure 3.4—there are many classes of neurons, neurochemicals, and potential mechanisms of information processing. Our first simplification, therefore, is to focus only on "integrate and fire neurons (see figure 3.3)." **The statement is astounding because it eliminates the granular cells of the brain from their considerations.** It is conservatively estimated (Section 10.1.2 & 10.1.3) that the granular cells constitute more than 90% of the brain cells in the central nervous system. They have eliminated these from their presentation!!! The number of granular cells increases periodically as more investigations using electron-microscopy count granular cells not resolvable using visual microscopes. In 2006, Buzsaki said on page 364, "There

¹Released: 1 August 2016

²Van Gelder, T. (1995) What might cognition be, if not computation? *J Phil* vol 151, pp 345-381

³Haikonen, P. (2009) The role of associative processing in cognitive computing *Cogn Comp* vol 1, pp 42-49

⁴Baars, B. & Gage, N. eds. (2007) Cognition, Brain, and Consciousness: Introduction to Cognitive Neuroscience. NY: Academic Press

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are more granule cells ($\sim 10^{11}$) than all neurons combined in the (human) neocortex.”

Baars & Gage provided a 2nd Edition of their book in 2010 that moved their above statement to page 65. The 2nd Edition includes a totally rewritten chapter 8, a major revision to chapter 12 and a new chapter 16 (related to the inferred effect of genes on the neural system based on relatively old interpretations). The preface describes these updates in more detail as necessary because the field is advancing like a “Big Wave” at Waikiki Beach. The book has an added Pull Out section at the front and an extensive Glossary at the rear which are both welcome and important additions. For the first time in a text, the resolution level of MRI techniques have allowed the LGN and the pulvinar to be identified and their relevance discussed (in the rewritten Chapter 8).

The new chapter stresses the two-way communications intrinsic to virtually all thalamo-cortical and trans-cortical commissure via the corpus callosum in line with the assertions of this work. The new Figure 8.10A and B are interesting with regard to the dorsal visual path. Frame A shows the thalamo-cortical paths identified by MRI but frame B relies upon a cartoon to identify the cortico-cortical paths (even though an associated inset does not justify the cartoon). They then note (page 250), “Keep in mind also that the thalamus is the major *input* hub for the cortex, and also the major cortex-to-cortex traffic hub. . . However, the basal ganglia operate as a major *output* hub, for motor control and executive functions.” The subject of two-way communications is also addressed on page 252 relative to vision with “In fact, about 90% of the LGN-V1 fibers are ‘running the wrong way’. **Above the LGN, everything is a two-way highway. This is a dominant feature of the brain, and it is a great challenge to understand how two-way connections work.**” The emphasis was added because of the critical importance of this statement. **It is in agreement with the hypothesis of this work.**

They continue to use two unifying diagrams to aid the discussions, a “Circle of Hierarchies” (page 2 and attributed to Drake et al⁵.) and a “Functional Framework” (Page 39). Both are excellent at the conceptual level but differ significantly. Neither includes a sector for gustation and the Functional Framework includes only vision, hearing and touch as sensory inputs. The Circle of Hierarchies does leave several sectors unidentified, suggesting they can be labeled by the reader if desired. Neither of these diagrams are included in their Pull Out section. The subject of a comprehensive saliency map is also included.

The 2nd Edition of Baars & Gage drops their identification as editors from the front matter, although they still describe themselves as editors on the last page of the rewritten preface. They do list a group of contributors in the preface, but no explicit authors are listed for the specific chapters.

Gurney has addressed the cognition task⁶. He has asserted that in cognition, “a very powerful stratagem is to ‘reverse engineer’ the brain and that computational neuroscience plays a pivotal role in this program.” In implementing this approach, he defined four levels; “computation, algorithm, mechanism and biological substrate.” He did not pursue levels three and four in depth. This author has used this stratagem over many years to tease out the operational relationships between elements of the neural system, down to his fourth level, the biological substrate level. There is a major unstated problem with the largely philosophical Gurney hierarchy. A computation, or an algorithm, or a mechanism cannot be used in a model unless it can be shown to be plausible at the biological substrate level. He makes no effort to demonstrate plausibility at the mechanism or biological substrate levels. While dealing primarily in symbolic logic, he makes no effort to describe the set of mathematical functions available to the neural system.

⁵Drake, R. Vogl, W. & Mitchell, A. (2005) Gray's Anatomy for Students. 3rd volume, Philadelphia, chapter 8, Head & Neck Section

⁶Gurney, K. (2009) Reverse Engineering the Vertebrate Brain: Methodological Principles for a Biologically Grounded Programme of Cognitive Modelling *Cogn Comput* vol 1, pp 29–41

These and other philosophical papers are of help in visualizing the operation of the cognitive system, they do not provide a viable framework, or understanding of the mechanisms occurring within the constraints of the biological physiology.

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While a variety of areas of the frontal lobe have been identified, primarily by electrical probing and/or traumatic lesion, the neural architecture of this lobe remains largely a mystery.. When an area has been identified, it has frequently been described as a pre-motor or pre-language area. In the context of this work, such titles need additional perfection to indicate they may be generating instructions destined for those parts of the efferent neural system, but they are not generating actual commands used in those elements.

The focus of this chapter is on the cognitive function (stage 5) generally associated with the area of the human brain forward of the precentral sulcus (Brodmann's areas 9-14) and generally labeled the prefrontal cortex. This area is particularly highly developed in higher primates. The area between the precentral sulcus and the central sulcus (primarily Brodmann's areas 4, 6, 43, 44 & 45) are generally described as premotor areas. These areas are generally associated with instruction generation associated with a variety of high level motor functions and will be associated with stage 6 in this work. Area 6 is frequently described as an area issuing high level, adversive, commands that cause the creation of multiple low level commands in area 4 particularly.

The above delineation leads to a suggested redefinition of the cytoarchitecture of the brain along functional rather than anatomical lines. The proposal is to define a region from the superior frontal sulcus to the occipital-parietal sulcus as a single *orofi* lobe to include areas 4, 6, 43, 44 & 45 along with the sensory integration areas of Brodmann areas 1, 2, 3 & 7 (**Section 10.2.1.1**). The *orofi* lobe defined in this way includes a majority of the information interface with the cognitive circuits of stage 5. The sensory interface is found posterior of the central sulcus. The motor interface is found anterior to the central sulcus. This area contains the regions often described as premotor. Premotor areas include prephonic, pretactile, pre-facile, pre-postural areas and the frontal eye fields. The supervisory interface with stage 5 would remain primarily with the thalamus. The role of the basal ganglia remains undefined in this framework. The label basal ganglia appears to be a catchall for neural elements whose purposes are poorly understood (**Section 12.5.2**).

This definition places Broca's area clearly in the stage 6 premotor area of the *orofi* lobe. Donaldson described the dorsal part of Broca's area as associated with writing text while the ventral area was associated with spoken language. While Broca's area has traditionally been considered to occupy both the gyri and sulci of areas 44 and 45, recent fMRI investigations are beginning to delineate the area of Broca more clearly and even define distinct subordinate roles to engines within the overall area^{7,8}. Conversely, Wernicke's area, generally described as occupying large parts of areas 22, 41, 42 and extending into areas 37 & 39, are clearly in the stage 4 information extraction region. More specifically, areas of 41 and 42 are associated with information extraction from speech within the hearing modality and areas of 37 & 39 are associated with textual information extraction from the vision modality.

Shallice (2004, pg 946) has observed, "Many different types of evidence support the idea that prefrontal cortex is involved in non-routine as opposed to routine operations." Barbas &

⁷Ullman, M. (2006) Is Broca's area part of a basal ganglia thalamocortical circuit? *Cortex* vol 42, pp 480-485

⁸Hillis, A. & Rapp, B. (2004) Cognitive and neural substrates of written language: comprehension and production *In Gazzaniga, M. ed. The Cognitive Neurosciences, Third Edition. Cambridge, MA: MIT Press Chap 55*

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Zikopoulos⁹, have asserted, "The prefrontal cortex is an action-oriented region, a feature generally associated with lateral prefrontal areas." These views are too narrow. The prefrontal cortex is the seat of cognitive activity of all types. It includes the examination of information supplied to it via the saliency map, the generation of extemporaneous volition instructions, and the associated abstract cognitive functions.

Mesulam has made a critically important observation. "As so many clinicians have observed, prefrontal lesions do not give rise to salient apraxia, agnosia, or aphasia, deficits that are easily documented by standard tests and bedside examinations. Instead, prefrontal lesions give rise to context-dependent impairments of judgement, insight, inference, decision-making, prioritization, perspective shifting, mental flexibility, and the ability to harmonize feeling with thought. The one common theme that I have been able to find among the numerous behavioral affiliations attributed to the frontal lobes is the transcending of what might be called a 'default mode' of neural processing¹⁰." This description is key. He goes on to define the characteristics of his default mode. A major goal of this work is to simplify his listing of characteristics and describe a "fundamental operational mode" that clearly differs from the definition of his "default mode." The fundamental mode would operate in the absence of any embellishments and irrespective of the source of the sensory information.

The circuit involved in high level motor functions are generating what are described as adverse instructions. Adverse instructions are high level instructions that tell the system to implement complex activities involving many individual neural/glandular functions. An example would be an adverse instruction to initiate the vowel "e." Such an instruction causes action in the pulmonary system, the larynx, the oral cavity, the tongue; and very likely the muscles of the neck and torso causing the subject to face the target of the communication. Adverse instructions also include a temporal component that aids in the implementation of the detailed instructions within stage 6.

High order adverse instructions may affect both sides of a bilateral animal. On the other hand, lower level adverse instructions may be seen to primarily affect the contralateral side of the subject. These instructions are sometimes described as antagonistic rather than contralateral.

As Noback (page 247) and others have noted, the prefrontal cortex is in excellent reciprocal communications with the dorsomedial nucleus of the thalamus. To reach the dorsomedial nucleus, the neurons necessarily pass through and communicate with the thalamic reticular nucleus (TRN) and the TRN is the probable source of timing information within the neurological system (page 239).

Fuster has updated his presentation on "The Prefrontal Cortex" in a recent 4th Ed¹¹. The work is comprehensive but addresses these structures largely from the psychological and behavioral perspectives. He notes on page 372, "The model is incomplete in terms of precise circuitry and computational operations, but is sufficiently detailed, structurally and functionally, to allow the testing of specific hypotheses, even in computational terms. His models are based primarily on first order traffic analysis at the histological level (examples, figures 2.13, 2.16 & 2.17) and behavioral changes resulting from trauma. No second order traffic analyses, showing the relative traffic volume between elements over recognized (first order) traffic paths, is provided. In line with his comment about precision, most of his schematics and block diagrams employ quite wide brush strokes.

⁹Barbas, H. & Zikopoulos, B. (2006) Sequential and parallel circuits for emotional processing in primate orbitofrontal cortex *In* Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press pp 57-83 page 73

¹⁰Mesulam, M. (2006) Forward *In* Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press.

¹¹Fuster, J. (2008) *The Prefrontal Cortex*. NY: Elsevier

12.1.1 Functional Background to cognitive operation

The bilateral character of the overall cortex is important in the understanding of cognition. The left and right hemispheres of the cerebral cortex are capable of operating independently in many animal species. "With training, the split-brain animal can use its two "half-brains" independently or simultaneously to perform different tasks. Each half-brain performs its own perceptual, learning and memory processes (Noback, page 250)." In the case of *Cetacea*, it is believed the two hemispheres are able to enter the sleep state independently. Although humans show some degree of dominance by one hemisphere or the other, the dominance is not overwhelming. Loss of one cerebral hemisphere, or one amygdala or hippocampus, does not significantly degrade the individuals performance in a wide range of skills including memory deposition, storage and retrieval. "When the corpus callosum is completely transected, even in man, no functional alterations can be detected, even after careful neurologic and psychologic examinations. Behavior patterns are not noticeably disturbed. Complex activities, such as playing musical instruments, typing, and writing, are performed with the same dexterity as prior to sectioning (Noback, page 249)." A somewhat different situation occurs in humans if the dominant lobe of the PFC is damaged (page 239). It may take an extended period for the subject to regain a high level of complex motor activity.

"The behavioral response of split-brained animals with ablated amygdala are informative. The bilateral removal of the amygdala converts an excitable, temperamental, and wild monkey into a placid and docile animal; whereas the unilateral removal of the amygdala produces little if any, observable change in a primate. A split-brain monkey (one with midline transection of the corpus callosum, anterior commissure and habenular commissure) with a unilateral ablation of the amygdala exhibits interesting behavioral responses. When an aggravating visual stimulus is presented to the eye on the side with the intact amygdala (with the opposite eye blindfolded), the monkey response is in an emotional, aggressive and belligerent manner. When the same visual stimulus is present to the eye on the side with the ablated amygdala, the monkey shows no emotional or aggressive response but remains docile and tame. This is in line with the concept that the commissure act to transfer information from one hemisphere to the other (Noback, page 250)."

Ablation of small areas of premotor area 6 does not result in paralysis. It merely eliminates some adverse instructions from the subjects repertoire (Noback, page 247). "Forced grasping and groping movements are attempted until the object is touched by the palm. After the grasp is firm, difficulty is experienced in releasing the object from the hand. The ablation of premotor area 6 and motor area 4 result in a flaccid paralysis with a slight increase in muscle tone." "The functional role of an ablated area of the cortex should not and cannot be objectively inferred from observations of the residual activity of the subject." This quotation is supported by more recent comments in Fuster related to lesions of the cingulate nuclei causing similar flaccid paralysis.

An example of the above assertion concerns Broca's area. "Lesions of Broca's area, especially of the left dominant hemisphere, may result in motor or expressive aphasia. More often these lesions lead to a transient speech defect. This loss of articulate speech occurs even though there is no demonstrable paralysis of any muscles associated with speech. Complete loss of articulate speech—the ability to say only several words, mispronunciation of common everyday words, or repetition of the same word over and over again— may be a consequence of the total destruction of Broca's speech area. At times these patients may express themselves with better facility when under emotional stress (Noback, page 249)." This ability strongly suggests stage 5 may utilize multiple parallel signaling paths like stage 4. These paths can provide significant backup capabilities. Barbas & Zikopoulos have reported "distinct clusters" of neurons trafficking between various stage 4 and stage 5 engines (page 73), particularly the executive regions of the prefrontal cortex and the thalamus. Lieberman has also spoken of these "groups of neurons" when discussing the higher order stage 4, 5 & 6 neural functions¹². These observations strongly suggest signaling using multiple parallel neurons carrying information in a word parallel/ bit serial format.

¹²Lieberman, P. (1998) *Eve Spoke*. NY: W. W. Norton page 105

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12.1.1.1 Postural configurations as possible adverse instructions

The control of the posture of an animal appears to be a good example of an adverse instruction. In their simplest form, they determine whether an animal walks on four feet, on two feet, or on two feet and uses its knuckles for additional support. In more complex forms, they determine the specific configuration of the animal during periods of stress. These postural configurations appear to be phylogenetic in character. A large human family in India appears to have a genetic defect that causes them to uniformly walk on their feet and knuckles (as do some of the larger apes)..

While the postural configuration appears to be controlled by an adverse instruction from the cognitive portion of the neural system, it is not clear where the memory template for these instructions is stored. It is worth considering whether these templates are stored as memories in an undefined area of the limbic system.

12.1.1.2 Coding used in the prefrontal cortex

Cook used a provocative and "grandiose title" for his 1986 book¹³. He discussed the subject in very conceptual terms. However, the fact remains that no code has been discovered describing the signaling used in the prefrontal cortex or any of the cerebral cortex forward of the central sulcus (except the fundamental stage 3, word serial/bit serial, code used in signal propagation, **Sections 9.2 and 9.3**). Cook focused on the anatomy of the CNS with some useful figures showing traffic flow among the principle sensory modalities.

12.1.2 Initial description of the prefrontal cortex

The computational power of stage 5 remains like that of the remainder of the CNS. It is primarily a pattern matching device. Like early man-made digital computers (through the 8080 and 6800 types), it does not have an internal capability to do transcendental mathematics (sines cosines, logarithms etc.). However, stage 5 has rapid access to a prodigious memory capacity and a significant learning capacity (creation of new memories, modified from previous memories).

The cognitive powers of any animal are fundamentally aligned with its survival. The fundamental cognitive function is to decide whether a threat in the external environment has been encountered before. If it has, the memories of the previous encounter are called for and compared to the present situation. If it has not, the first order conclusion is to withdraw from the situation. All subsequent decisions are based on this fundamental decision. If new information relative to the environment is received faster than stage 5 can process it to a satisfactory go-no go decision, the default response is withdrawal. The information rate is a product of the complexity of the total presentation presented to stage 5 at the saliency map. Thus, the information rate is the sum of the rates associated with the complexity of the information associated with each sensory modality.

If the above "remain or flight" decision is flight, a series of adverse instructions are generated and passed to the efferent neural system for implementation..

If the above "remain or flight" decision is to remain, the next decision involves interfacing with the threat. This interface could involve fighting or communication (in one form or another). Generally, the first action is an aggressive communications or an indication of a formidable defensive capability. The selected response appears to be arrived at following consultation with the amygdala as to the character of the response and the posture to be assumed prior to the response. The amygdala forms the entry point into the limbic system, commonly thought of as the seat of emotion in the CNS. The elements and features of the limbic system are difficult to define with precision.

¹³Cook, N. (1986) *The Brain Code*. NY: Methuen

In the case of oral communications, the sophistication of the communications can increase exponentially (to the level of romantic poetry, etc. in the case of man).

12.1.2.1 Cytoarchitecture of the prefrontal lobe

Descriptions of the prefrontal lobe are in flux, primarily because of the arrival of the fMRI as a viable research tool. The transition is moving toward the functional description of the lobe using coordinates compatible with this scanning technique rather than the coarse descriptions evolved from Brodmann in the 1910's. This labeling is also superceding a wide range of labels for small regions of the lobe based on spatial terms, lateral, orbital, rostral etc.

It is rare to find a graphic showing the frontal view of the cerebral cortex, especially the underside. Price has been a leader in this field¹⁴. Fuster has provided a first order labeling of the prefrontal cortex in **Figure 12.1.2-1**.

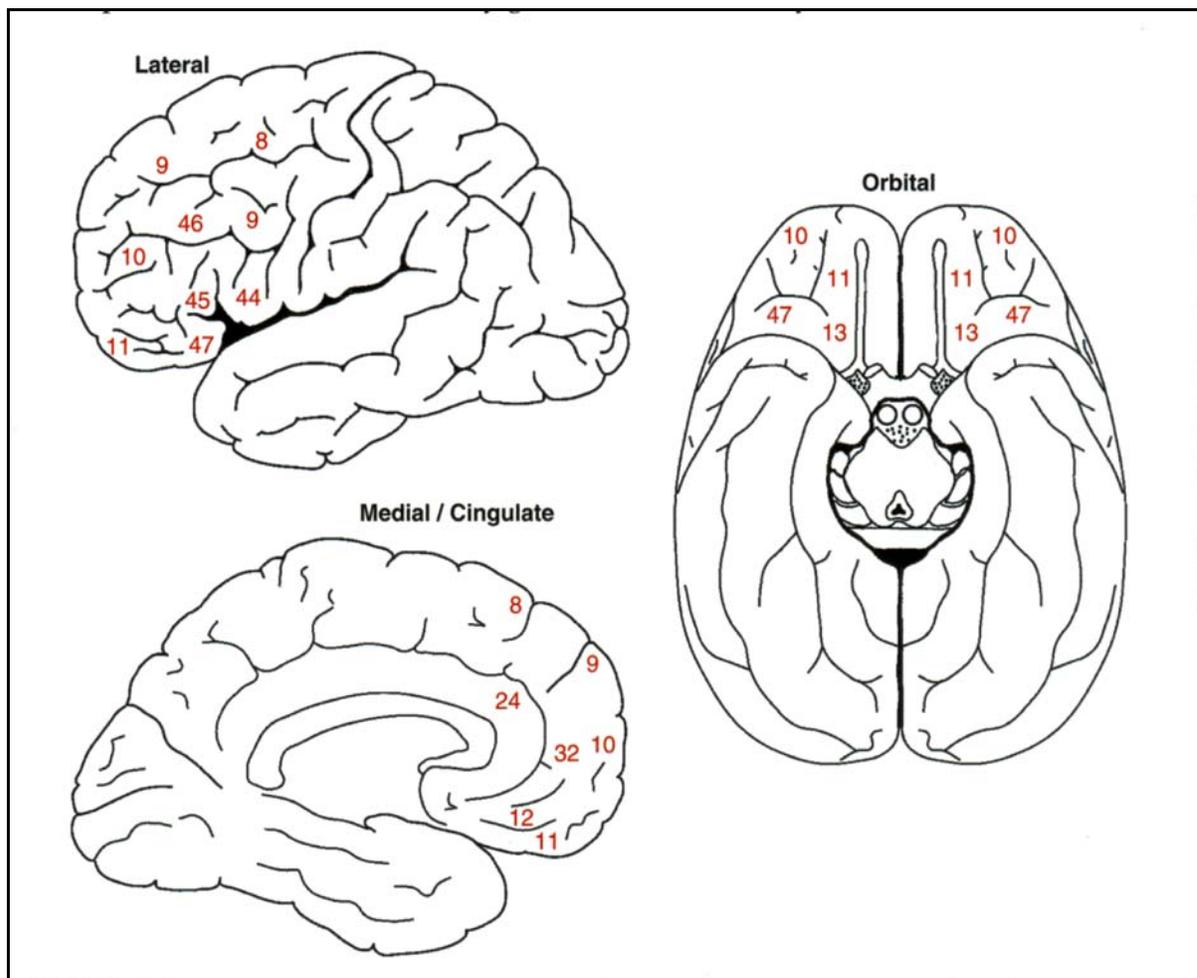


Figure 12.1.2-1 Lateral, orbital and medial views of the cortex focused on the prefrontal regions with numbering following Brodmann's cytoarchitectonic map. From Fuster, 2008.

¹⁴Price, J. (2006) Architectonic structures of the orbital and medial prefrontal cortex *In* Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press Chap 1.

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Figure 12.1.2-2 shows the nomenclature for the cytoarchitecture of the prefrontal lobe as recently expanded by Ongur et al¹⁵. Their focus was on the structure of the human orbital and medial prefrontal cortex (OMPFC) and used five histological and immunohistochemical stains. They used a variety of stains in an attempt to isolate and identify various regions and correlate those regions with similar regions in monkey.

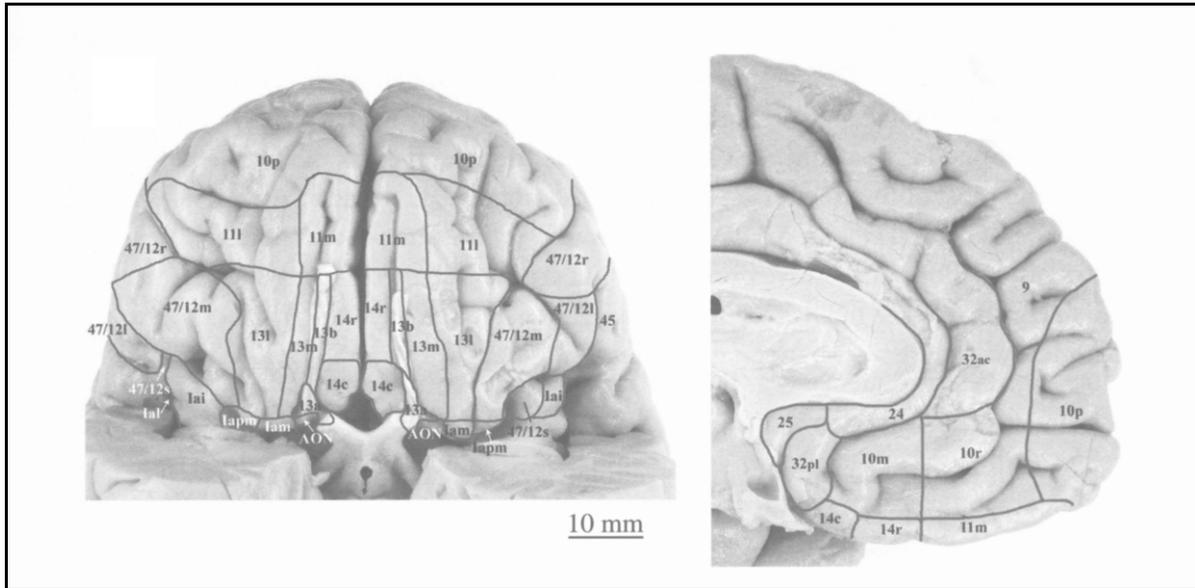


Figure 12.1.2-2 Architectonic maps of the orbital and medial prefrontal cortex in humans. As in the map by Petrides & Pandya (1994), the ventrolateral convexity in humans was designated area 47/12. From Ongur et al., 2003.

¹⁵Ongur, D. Ferry, A. & Price, J. (2003) Architectonic subdivisions of the human orbital and medial prefrontal cortex *J Comp Neurol* vol 460(3), pp 425-449

Figure 12.1.2-3 shows a preferred map of the right prefrontal cortex that has been flattened. The flattening necessarily distorts the dimensions of the presentation. The area labeled 47/12 is a compromise introduced by Petrides & Pandya in 1994 to designate a single functional area labeled 47 in human and 12 in monkey.

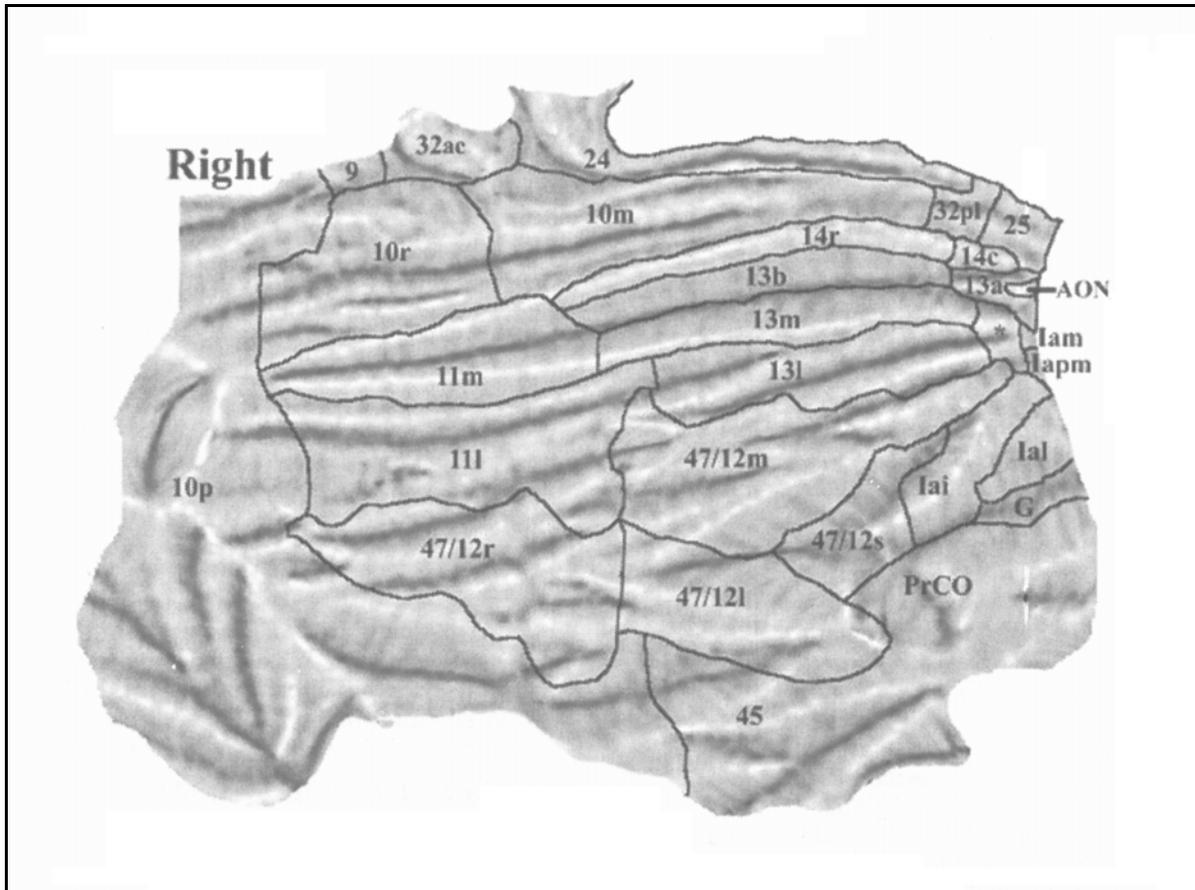


Figure 12.1.2-3 Flat map of the *right* human OMPFC. Constructed using the program CARET. The map is "cut" at the level of the corpus callosum, with the dorsal cortex not represented. The area marked with an asterisk is a region of conversion between areas 13m, 13l, and 47/12m, where it is difficult to assign an areal designation. AON; anterior olfactory nucleus. G; gustatory nucleus. PrCO; precentral opercular area. Pu; putamen. From Ongur et al., 2003.

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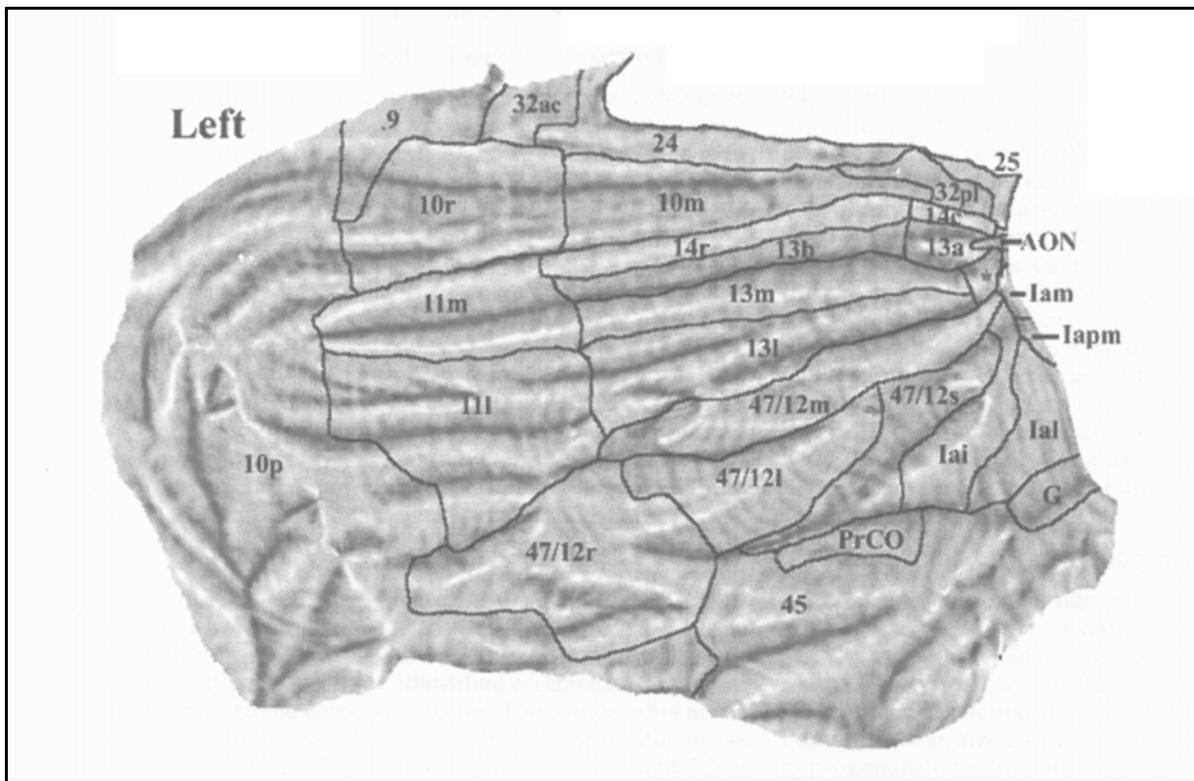


Figure 12.1.2-4 Flat map of the *left* human OMPFC. The area marked with an asterisk is a region of conversion between areas 13m, 13l, and 47/12m, where it is difficult to assign an areal designation. Constructed using the program CARET. The map is "cut" at the level of the corpus callosum, with the dorsal cortex not represented. AON; anterior olfactory nucleus. G; gustatory nucleus. PrCO; precentral opercular area. Pu; putamen. From Ongur et al., 2003.

The matching left side of the flattened map of the human brain is shown in **Figure 12.1.2-5**. The left and right figures have been arranged to highlight their symmetry and/or lack thereof. In fact the two areas adjacent to the corpus callosum (shown at upper right in both figures) should be adjacent to each other.

The right view appears to be a mirror image of the actual profile viewed from outside of the brain. Areas 24 and 25 are continuous between the two figures. The flattened maps are inconsistent with the earlier figure from Ongur et al. in the vicinity of area 32pl.

The precentral opercular area (PrCO) was labeled uniquely in the left prefrontal cortex by Ongur et al. but not separated from area 45 in the right prefrontal cortex. The role of the PrCO was not discussed in the 1998, 2000¹⁶ or 2003 papers. The specified area appears to be similar to area 46 of Brodmann. Carmichael & Price discussed the PrCO briefly in 1996, but not its functional role¹⁷. The areas marked G were generally associated with the gustatory modality.

Shallice has commented, "The prefrontal cortex is internally highly complex, with major

¹⁶Ongur, D. & Price, J. (2000) The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans *Cerebral Cortex* vol 10, pp 206-219

¹⁷Carmichael, S. & Price, J. (1996) Connectional networks within the orbital and medial prefrontal cortex of macaque monkeys *J Compar Neurol* vol 371, pp 179-207

functional differences between the lateral, orbital, and medial surfaces, along with increasing abstraction of function as one moves toward the frontal pole. This work would support this assertion without reservation. Ongur et al. propose the demarcated areas in their figures represent functionally separate areas based on their traffic analyses. If the proposal is correct, the question remaining is what are the functions of these areas? Ongur et al. used their Nissl stain most widely but used a modified Gallyas stain to identify myelinated fibers.

In anticipation of the expansion of Shallice's idea, it may pay to tentatively subdivide stage 5 at this point into:

Stage 5a- Recall & Evaluation by the PFC

Stage 5b- Cognition & Decision by the PFC and

Stage 5c- Action planning & Volition Instruction generation.

In this context, stage 5c would be in intimate contact with stage 6, adversive instruction generation.

While not of interest here, Ongur et al. assert that all of their demarcated areas have equivalent areas in the monkeys. This correlation may need to be examined at a more detailed level based on this work. It may be more true for orangutan than for monkeys (**Appendix D**).

Zald & Rauch have edited a new book that provides a large amount of information comparing the old nomenclature with the new and providing new results from recent fMRI scanning¹⁸. Their chapter 12 provides a figure on page 309 that is very helpful in relating many of the descriptive names of the frontal lobe with the more detailed cytoarchitectural names of Ongur, Price and others. The figure on page 327 shows the areas most associated with "visceral response and decision making," a rather general description. The area was previously described as the ventro-medial prefrontal cortex (VMPFC) or the orbitofrontal cortex (OFC) depending on the investigator, even though they do not refer to identical areas. According to Naqvi et al¹⁹, "the VMPFC excludes lateral portions of the OFC, namely area 47/12, as well as more dorsal and posterior regions of areas 24 and 32 of the medial prefrontal cortex." They illustrate the region beautifully based on psychological evaluations of brain injuries.

Petrides & Mackey also provide another figure on page 20-23 showing why the cytoarchitectural names, based on sulci and gyri are so inadequate. However, they do introduce an early table where the locations of individual sulci are specified by "bounding boxes" based on Montreal Neurological Institute (MNI) coordinates,²⁰ a follow-on to the Talairach & Touroux coordinates. They did not discuss the effect of a missing sulci in their calculations. In Chapter 3, Price begins to describe the interconnections within the prefrontal lobe and other neural engines based on the expanded descriptions of the locations of the engines of the prefrontal lobe. Chapter 6 contains a broader ventral view of the cerebral cortex than found previously (page 127). Page 132 shows a statistical plot of fMRI responses to a given olfactory stimulus from 12 separate trials. Based on this data, a very early statistical description of this area of the prefrontal lobe is given with mean and standard deviation dimensions.

12.1.2.2 Characteristics of cytoarchitectural areas

Ongur et al. have provided considerable data on the character of each of their areas. They

¹⁸Zald, D. & Rauch, S. eds. (2006) *The Orbitofrontal Cortex*. Oxford: Oxford Univ. Press

¹⁹Naqvi, N. Tranel, D. & Bechara, A. (2006) Visceral and decision-making functions of the ventromedial prefrontal cortex *In* Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press. Chap 13

²⁰Evans, A. Kamber, M. Collins, D. & MacDonald, D. (1994) An MRI-based probabilistic atlas of neuroanatomy *In* Shorvon, S. ed. *Magnetic resonance scanning and epilepsy*. NY: Plenum Press pp 263-274

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begin by defining two networks of interconnected areas from the earlier work of Ongur & Price²¹; the 'orbital' network receives and appears to integrate activity from several sensory modalities, whereas the 'medial' network has outputs to the hypothalamus and brainstem and appears to modulate visceral function. They cite a variety of investigators suggesting the medial network is associated with mood and visceral activities. They also cite a series of papers by Carmichael & Price for evidence of physical modularity and different input-output connections for these modules (engines in this work).

Fuchs & Phillips have provided some information on the paths of the commissure to and from the prefrontal lobe²². They suggest the dorsolateral areas receive inputs from a variety of sensory modalities via long intracortical pathways. They also provide some information on related to variations in language ability in the face of lesions to the prefrontal areas.

Figure 12.1.2-5 summarizes the data from the Ongur et al. paper. The nomenclature is nominally theirs. As noted earlier, the conventional use of "horizontal" in histology refers to a feature that is in fact parallel to the pia matter surface, regardless of the orientation of that surface. The terms radial and tangential would be more precise in most cases when talking about vertical and horizontal features. Radial and tangential would also be compatible with the corticogenesis theory of Rakic and colleagues²³. Ongur et al. use the term ramus and rami to refer only to branches of sulci and not branches of neurons or nerves. Most of their data is based on Nissal stains to identify soma of neurons with some use of Gallyas' stain to identify myelination. This stain makes the myelin of the white matter appear dark, which can be confusing in discussions. Many of the images provided by Ongur et al. contain subtle variations not easily recognized by the untrained eye. Comments here relating to these images will be limited.

²¹Ongur, D. & Price, J. (2000) The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans *Cereb Cortex* vol 10, pp 206-219

²²Fuchs, A. & Phillips, J. (1989) Association cortex *In* Patton, H. Fuchs, A. et al. eds. Textbook of Physiology, 21st Ed, Vol. 1. Philadelphia, PA: Saunders pp 677 & 686-687

²³Rakic, P. (1995) A small step for the cell—a giant leap for mankind: a hypothesis of neocortical expansion during evolution *Trends Neurosci* vol 18, pp 383-388

Table of putative Engine features										
Area #	"Network"			Baillarger's		Granularity		Myelin.	Plexus	Criss-cross
	Orbital	Medial	? Interface	Inner	Outer	agran.	dys-			
10m		**								**
10o										
10p		**								**
10r		**								**
11l	**									
11m			**							
12l										
12m										
12o		**								
12r										
13a			**			**				
13b			**				**	Rad & H.		**
13l	**						**	**		
13m	**						**	Rad & III		
14c			**							
14r			**							
24a						**				
24b		**				**				
24c										
25		**				**				
32										
32ac						**				
32pl		**				**				
47/12l	**			**	**			**	II	
47/12m	**			**	**			**	II	
47/12r	**			***	**			**		
47/12s		**								
lai		**				**				
lal	**					**	**	**		
lam	**					**			I	
lapm	**					**				

Figure 12.1.2-5 Prefrontal lobe area characteristics according to Ongur et al. Summarized from their written text using their nomenclature. From Ongur et al. 2003.

The identification of the myelinated axons as stage 3 projection neurons in **Section 9.1.1** of this work aids considerably in determining the function of many neural areas. The description of the primary paths of these myelinated neurons, as described in **Section 10.1.2**, is also an aid.

12.1.2.2.1 "Crisscross" regions within specific areas

Ongur et al. identify multiple "crisscross" areas characterized by myelinated fibers traveling both horizontally and radially in the same region of a cross section of cerebral cortex. They

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note this condition in layers III and V of area 13b and the dysgranular character of layer IV. They also note its presence in areas 10m, 10r and 10p where they suggest it may appear in layers III, IV & V, which distinguish these areas from area 11l and 47/12r.

The significance of this structure, if any, has not been determined. The crisscross expression has not been found elsewhere in the literature. The crisscross pattern is unrecognizable by this analyst in figure 15 of Ongur & Price.

12.1.2.2.2 Plexuses of significance by area

Ongur & Price do not define their terminology precisely with regard to "fibers" and "neurites." These terms will be taken to mean axon segments and neurites (either dendrites or podites) of neurons as defined in **Section 2.2**. They note a strong plexus of such fibers and neurites in layer III of areas 13b, 13m and 13l (page 435). Such structures are strongly suggestive of a special purpose for this area, particularly if the neurites were of the long type they discussed in general on page 429.

Ongur & Price briefly describe a "double plexus" on page 446 found in layers 24a, 24b & 25.

12.1.2.2.3 The role of the "networks" in the prefrontal lobe

Figure 12.1.2-6 shows a partitioned left prefrontal lobe based on the "networks" defined by Ongur et al. based on an interpretation of their staining studies. "The orbital network involves most of the areas on the orbital surface. It receives and integrates sensory information from several modalities." Price (2006, page 52) suggests the orbital network receives information from all, or almost all, of the sensory modalities. He indicates the medial network does not have obvious sensory inputs but is focused on the hypothalamus and brainstem. The medial network involves areas on the medial wall and also areas at the lateral edge of the orbital cortex. These areas project to visceral control centers in the hypothalamus and periaqueductal gray." The areas on the tip and lateral edge of the gyrus rectus are at the junction between the two networks and are somewhat associated with both; they may serve to transfer information between the networks." These networks are still defined primarily on the basis of geography and only secondarily with respect to function.

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stratified neuron. Both frames a & b are labeled as Purkinje Cells even though a is bi-stratified while b appears to be an example of an amercine neuron. The introduction provides a nice pictorial record of historical workers in the field. The comments relative to the glial cells of the brain are superficial (page 35). They do note the potential role of astrocytes as neurons themselves (as suggested by their illustration, Fig 2.15). They do provide a nice artist's illustration of the gross anatomy of the spinal cord and adjacent tissue. An exploded view of the pulvinar in Fig 2.24 is nice but only introductory. Fig 2.37 attempts to illustrate the primary sensory information extraction areas but without significant annotation. Figure 1 on page 59 was apparently added in a hurry since it is not numbered in proper order. It shows a variety of coronal views of brains from a broad assortment of animals. They do address several variants of the Stroop Effect on page 77, but briefly. Table 3.1 addresses the most obvious characteristics of several common neural diseases, primarily degenerative and potentially infectious disorders. On page 116, they have inserted a figure 3.41 modified from one presented by Churchland in 1993 without any attribution or discussion. They do illustrate the crude resolution of transcranial magnetic stimulation (TMS), typically a voxel of 1cm³.

Miyake et al. have provided a broad study of what they define as three major executive tasks of the "Frontal Lobe" using latent variable analysis techniques.²⁷ This individual differences study examined the separability of three often postulated executive functions—mental set shifting ("Shifting"), information updating and monitoring ("Updating"), and inhibition of prepotent responses ("Inhibition")—and their roles in complex "frontal lobe" or "executive" tasks. They note on page 84, "Although the statistical models evaluated in this article are relatively simple, the interpretations of the CFA and SEM results critically hinge on our assumption that the three latent variables in these models indeed succeeded in tapping the three target executive functions (i.e., Shifting, Updating, and Inhibition, respectively). Any violations of this assumption would seriously challenge the conclusions we drew from the CFA and SEM results. Therefore, it is important to rule out alternative explanations that question the validity of that assumption." [xxx evaluate their approach—on memory stick]

Humphreys & Samson have presented material on the phenomenon of attention and the frontal lobes²⁸. [xxx review this] They note the interplay of the prefrontal areas with the frontal eye field and the superior colliculus. Treisman has presented additional material on selective attention²⁹. [xxx expand]

Shimamura et al³⁰.

Shallice has reviewed the efforts to relate the prefrontal lobe to the supervision and control of the conscious operations of the neural system³¹. Although progressive and usefully suggestive, the level of abstraction is high compared to that used to describe the neural system up to this point.

²⁷Miyake, A. Friedman, N. Emerson, M. Witzki, A. Howerter, A. & Wager, T. (2000) The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: a latent variable analysis *Cogn Psych* vol 41, pp 49–100

²⁸Humphreys, G. & Samson, D. (2004) Attention and the frontal lobes *In Gazzaniga, M. ed. (2004) The Cognitive Neurosciences, 3rd Ed. Cambridge, MA: MIT Press Chap. 44*

²⁹Treisman, A. (2004) Psychological issues in selective attention *In Gazzaniga, M. ed. (2004) The Cognitive Neurosciences, 3rd Ed. Cambridge, MA: MIT Press Chap. 39*

³⁰Shimamura, A. (1995) Memory and frontal lobe function *In Gazzaniga, M. ed. The Cognitive Neurosciences. Cambridge, MA: MIT Press pp 803-813*

³¹Shallice, T. (2004) The fractionation of supervisory control *In Gazzaniga, M. ed. (2004) The Cognitive Neurosciences, 3rd Ed. Cambridge, MA: MIT Press Chap. 68*

12.1.3.1 Clinical syndromes of prefrontal cortex trauma

Fuster has discussed the three major syndromes recognized clinically as resulting from trauma to the prefrontal cortex. First, the lateral syndrome, associated with trauma to parts or all of areas 8, 9, 10 and/or 46 individually. The lateral syndrome is dominated by an attention disorder. "At its foundation seems to be a lack of drive and awareness. Patients are generally apathetic, disinterested in themselves and the world around them." The orbito-frontal syndrome involves trauma to areas 11 and/or 13. The subject is unable to "focus attention and simultaneously suppress interference from external stimuli or internal tendencies." Apathy is the dominant characteristic of the third, medial/anterior syndrome. However damage to areas 8 through 10 and areas 12, 24 & 32 also exhibit difficulties in eye, limb or speech movements.

12.1.3.2 Kindling, an electro-physical clinical technique

"Electrical kindling is the process by which a previously sub-convulsive stimulus comes to induce convulsive behavior when applied repeatedly and intermittently to selected areas of the brain³²." "Kindled seizures can be induced gradually and under precise experimental control." As such, "Kindling is an experimental paradigm used to model temporal lobe epilepsy." "The most sensitive areas from which to elicit epileptiform activity include such limbic areas as the amygdala, . . ." Weiss et al. give both a more extensive and detailed description of the individual stages of biological activity elicited by kindling.

12.1.4 Efforts to simulate the operation of the prefrontal lobe

After examining many aspects of the functioning brain, Edelman prepared a flow diagram used in an extensive simulation of brain operation³³. He initially defined a Darwinian computer as opposed to a Von Neuman computer or a Turing engine. He compared a single stimuli with a repertoire of potential memories before addressing the problem of determining the best fit. The flow diagram in his Appendix A appears to be in line with the operation of the brain envisioned here, except for his use of binary stimuli instead of continuous analog stimuli.

Fuster notes the ability to record evoked-potentials from the prefrontal cortex and a not unexpected result (page 235), "Walter and associated discovered that practically any sensory stimulus can elicit a protracted surface-negative potential over the same region *if*, by training or verbal instruction, the stimulus has acquired behavioral significance."

12.1.5 Recent studies using brain imaging techniques

Henson et al. have provided fMRI images of brain activity when presented with a series of individual words³⁴. Their hypothesis was "that one role of the right prefrontal cortex is to monitor the information retrieved from episodic memory in order to make an appropriate response."

They measured BOLD oxygen levels with sampling intervals in the 40 ms range. They note the natural tendency to relate these words to stored memories relating to these words. [xxx expand] One interpretation of their remarks is that, the prefrontal controller/monitor is focused in BA 46. Alternately, one of the controllers of the short term memory acquisition and recovery elements may be in BA 46

³²Weiss, S. Sitcoske-O'Shea, M. & Post, R. (2000) Amygdala plasticity: the neurobiological implications of kindling *In* Aggleton, J. ed. *The Amygdala*. NY: Oxford Press Chapter 4

³³Edelman, G. (1981) Group selection as the basis for higher brain function *In* Schmitt, F. Worden, F. Adelman, G. & Dennis, S. eds *The Organization of the Cerebral Cortex*. Cambridge, MA: MIT Press Chap 22

³⁴Henson, R. Shallice, T. & Dolan, R. (1999) Right prefrontal cortex and episodic memory retrieval: a functional fMRI test of the monitoring hypothesis *Brain* vol 122, pp 1367-1381

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Recently, questions have arisen about how accurately the BOLD technique describes the location of actual neural activity. Walters et al.³⁵ noted, "as fMRI records changes in blood oxygenation, the functional activation may have spilled into other regions. An important issue is to what extent do activation foci correspond to architectonic fields." Thus they speculate the fMRI imagery may reflect areas of oxygen variation that are larger than the area of functional interest. This problem will become a bigger problem as MRI equipment with magnets stronger than 4.7 Tesla (and a bore of 30 cm) and shorter sampling times become available.

As noted by Adolphs et al. fMRI with a 3.0 Tesla magnet still exhibits a resolution about 100 times less than achievable with electrophysiological probing³⁶.

As discussed in Chapter 3, the oxygen level in the local blood supply is directly associated with the homeostasis of the cells in that region (metabolic consumption) but is only indirectly associated with the level of neural activity. The more direct measure of neural activity is the rate of electrical power consumption and hence the rate of consumption of the neurofacilitator, glutamic acid (glutamate) or the rate of generation of the byproduct of the electrostenolytic process, GABA. Oxygen utilization for purposes of glutamate generation is called metabotropic consumption. Glutamate is formed by the partial oxidation of glycogen and a time constant is involved that may still impact future fMRI measurements with short sampling intervals. However, this time constant will always be shorter than that associated with the multi-step conversion of glycogen plus oxygen into electricity.

Waites et al. have reported on the combining of simultaneous EEG and fMRI imaging³⁷. [xxx expand]

A new technique, magnetic resonance spectroscopy (MRS) is beginning to provide new information about the neural system³⁸. The technique is particularly useful in mapping glutamic acid (glutamate) within the CNS. As Herrington noted (page 334), "Unlike other forms of spectroscopy, the physics underlying MR spectroscopy offers the unique ability to 'engineer' acquisition methods to optimize the measurement of different compounds."

As discussed in Chapter 3 (Power Supply), the glutamate-glutamine cycle and the glutamine-GABA cycle do not play major roles in the neural system as suggested by Petroff (page 352). The glutamate-GABA cycle he suggests potentially exists (page 360) is not used in the neural system. It is replaced by the glutamate to GABA conversion occurring in the electrostenolytic process powering the neurons. This process is not enzyme driven. It is a stereochemical reaction occurring only at specific sites on the external surface of each neuron. Although he uses the term unique to describe several of the above loops in his conceptual discussion, none are as unique as the role of the only two negatively charged amino acids (glutamic acid and its backup aspartic acid) in powering the neural system. Without these two entities, the negative voltage required to operate the neural system would not exist.

³⁵Walters, N. Egan, G. Kril, J. Kean, M. et al. (2003) In vivo identification of human cortical areas using high-resolution MRI: An approach to cerebral structure–function correlation *PNAS* vol 100(5), pp 2981–2986

³⁶Adolphs R. Kawasaki, H. Oya, H. & Howard, M. (2006) Intracranial electrophysiology of the human orbitofrontal cortex *In* Zald, D. & Rauch, S. *eds.* The Orbitofrontal Cortex. Oxford: Oxford Univ Press. page 357

³⁷Waites, A. Abbott, D. Fleming, S. & Jackson, G. (2005) Magnetic resonance neurophysiology: simultaneous EEG and fMRI *In* Kuzniesky, R. & Jackson, G. *eds.* Magnetic Resonance in Epilepsy. NY: Elsevier Chap 11

³⁸Hetherington, H. Petroff, O. Jackson, G. Kuzniecky, R. Briellmann, R. & Willard, R. (2005) Magnetic resonance spectroscopy *In* Kuzniesky, R. & Jackson, G. *eds.* Magnetic Resonance in Epilepsy. NY: Elsevier Chap 13 (In three parts)

The role of lactate in the production of glutamic acid is also discussed in Chapter 3. The level of lactate in the brain seems highly correlated with epileptic activity. The low concentration of GABA during epileptic events seems easily correlated with the rise in lactate level. Both would suggest "cutoff" in the operating characteristics of many neurons in the affected area. Jackson et al. have gathered valuable evidence that is compatible with the operation of the neural system discussed earlier in this work³⁹. [xxx expand]

12.1.5.1 Comparing archaic and modern energy consumption calculations

Laughlin has provided an analysis of the oxygen consumption of the brain to expand understanding of the BOLD process/mechanism⁴⁰. However, he has only provided gross calculations based on questionable assumptions, especially the use of the Huxley and Hodgkin concept of a chemically driven neuron.

Laughlin's assumptions include;

- the human retina and gray matter of the brain, along with the heart, consumes 10-30 times the bodies resting average energy consumption.
- "the human brain consumes energy at a high rate that is little changed by mental activity."
- "Cortical gray matter apparently uses more energy for signaling than most other regions of the brain."
- "Because approximately 90% of cortical synapses use glutamate, the correlation between glucose consumption and glutamate turnover associates changes in metabolic rate with changes in neural activity."
- "The deepest anaesthesia abolishes both electrical activity and the turnover of glutamate, and depresses glucose consumption by 80%-90%."

Laughlin identifies several theoretical approaches to calculating the energy budgets for neural signaling. He settles on what he identifies as the "Bottom Up" approach. Laughlin summarizes the difficulty of his chosen problem on page 189. "The ideal solution to this problem is to use anatomical and physiological data to estimate the synaptic drive, but this involves an exceptionally detailed knowledge of circuitry that is not yet available in cortex." "Cortical energy budgets circumvent this problem by considering the average cortical neuron firing at the average rate because it is being driven by the average number of synapses."

His last sentence illustrates the problem with his method. He assumes all cortical neurons generate action potentials.

Laughlin calculates his consumption of glutamate per neuron based on a set of chemical equations that are not identified. He actually estimates the energy consumption based on a rate of ATP consumption relying upon the Huxley and Hodgkin model of a chemically-based neuron. A major problem with energy balance calculations is they do not consider the polarity of the energy transferred. While not critical in strictly chemical reactions, it is critical in electrostenolytic reactions. Only glutamate and aspartate are capable of creating a negative potential inside a cell membrane.

Implementing his gross budget leads to an average action potential firing rate for each neuron of 3 to 5.5 pulses per second. This is clearly an impossibly low number under the assumption that all cortical neurons generate action potentials. Most neurons generating action potentials exhibit a resting pulse rate of 10 to 30 pulses per second with active rates in the 100 to 600 pulses per second range. Based on the critical flicker frequency of vision (nominally 30 frames/sec), it appears the brain operates with an effective frame time on the order of 30 msec. This suggests the action potential rates of information carrying channels

³⁹Jackson, G. Kuzniecky, R. Briellmann, R. & Wellard, M. (2005) Clinical applications of magnetic resonance spectroscopy in epilepsy *In* Kuzniescky, R. & Jackson, G. eds. *Magnetic Resonance in Epilepsy*. NY: Elsevier Chap 13 pages 370-383

⁴⁰Laughlin, S. (2004) The implications of metabolic energy requirements for the representation of information in neurons *In* Gazzaniga, M. ed. *The Cognitive Neurosciences*, 3rd Ed. Cambridge, MA: MIT Press Chap 14

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exceeds 30 pulses per second.

Laughlin's figure 14.3 suggests transmission rates exceeding 2500 bits/second. This is an unrealistic and undocumented action potential rate for any neural circuit. See **Section 9.3.3**.

Laughlin recognizes the pulse rate limiting constraints in his calculations (page 192) and offers several alternatives. First, combine analog and digital signaling in hybrid circuits. Second, splitting signals into parallel lines. Third, eliminating redundant synapses. The first suggestion is the actual technique used in the cortex. However, Laughlin's analyses encounter serious problems as he notes on page 188, "The average [energy consumption] for gray matter is approximately 50% higher than the specific metabolic rate of the whole brain." "The lowest rates [of consumption] are in white matter." It is only in the white matter of stage 3 neurons that action potentials are encountered. No action potentials are associated with gray matter.

Laughlin provides several useful estimates of gross energy use per unit volume of brain material. However, the "gray matter" tissue of the brain is formed in a laminar sheet. While the energy consumption of this matter can be given on a per unit volume basis at histological scale, it cannot be given in per unit value basis so easily for larger volumes where the consumption is on a per unit area basis and following the curvature of the cortex.

Laughlin's analyses can be salvaged by recognizing that less than 5% of the cortical neurons are stage 3 neurons generating action potentials (white matter) and these stage 3 neurons are very economical energy-wise. The bulk of the neurons of the cortex are stage 4 and stage 5 analog neurons.

Laughlin's conclusion is totally correct but for the wrong reasons. "The energy required for signaling limits the number of action potentials available to the brain, and the brain counters this limitation with energy-efficient circuits, codes and representations."

An alternate to Laughlin's conclusion can be expressed more positively from a design perspective.

The cortex employs a variety of energy-efficient circuits, codes and representations in order to achieve minimum energy consumption in total and per unit volume.. Where signals are required to travel more than two millimeters, stage 3 action potential generating commissure (white matter) are used to minimize energy consumption per unit distance. These commissure use only about 5% of the total cortical energy. The remainder is consumed by the other 95% of the neurons (dark matter) acting in the analog mode.

Glutamic acid (glutamate) is the neuro-facilitator in the electrostenolytic reaction powering the system. It is not a neurotransmitter. Electrons are the nominal neurotransmitters passing through synapses (**Section 2.4**).

12.2 A "fundamental mode" of prefrontal cortex operation

Following the ideas of Edelman in 1980 and the earlier material in this book, it is possible to begin the definition of a functional block diagram of the executive (cognitive) portion of the brain. Goldberg & Bougakov have provided a largely conceptual block diagram showing the major connections to the prefrontal cortex based on Squire et al. (2003). Only selected external sensory modalities are shown. Many of the signal paths are also generic. It omits the stage 4 information extraction circuits and the saliency map of this work. A further modification of Squire is shown in of **Figure 12.2.1-1** Most of the connections in this figure are believed to involve multiple neuron commissure employing word serial-bit parallel signaling. Most of the connections are determined by traffic analysis following traumatic injuries. As developed in **Section 4.2.4**, many responses to sensory inputs derived from the alarm mode of signal processing are processed via the reflex path and can be implemented in Stage 6 command development circuits before the prefrontal cortex is aware of the event.

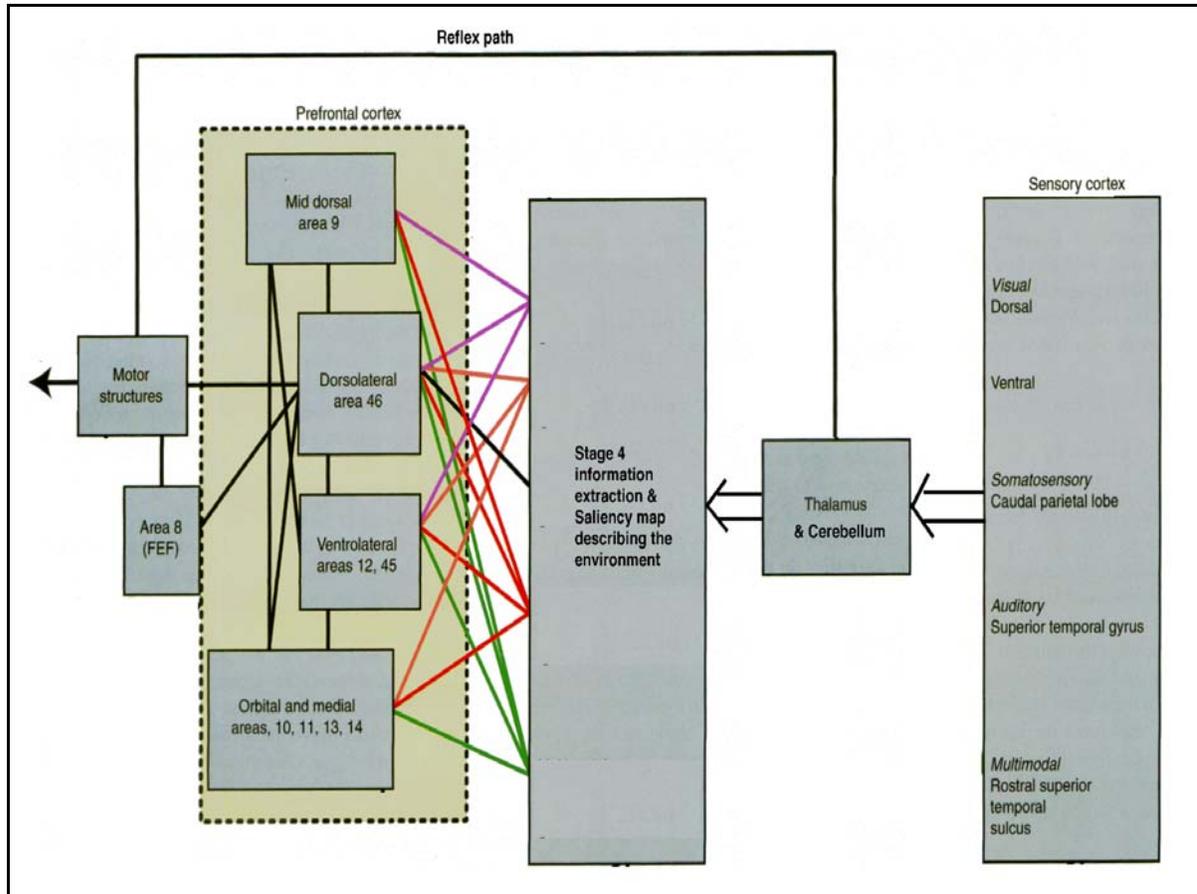


Figure 12.2.1-1 The major connections of the frontal lobes according to Squire et al. The colored lines are notional and are not all active simultaneously. The number of output ports available on the saliency map is unknown. A reflex path is shown from the thalamus and cerebellum of stage 4 to the motor circuits of stage 6 & 7. See text. Modified from Goldberg & Bougakov, 2008, as attributed to Squire et al., 2003.

Section 4.2 of Baars & Gage describe how they define the various engines of the prefrontal cortex based on Brodmann's area maps.

Figure 12.2.1-2 shows a similar initial block diagram, based on this work, describing the proposed fundamental mode of operation irrespective of the sensory material presented to it. The goal of this figure is to describe to the greatest extent possible what inputs and outputs are expected of the executive based on the known external topology of the CNS. The figure is delineated into the stages defined previously in this work but recognizes a potential need for an expansion. The work has not previously addressed the emotion aspects of the neural system, typically associated with the limbic system, explicitly, or the location of long term memory (LTM). It may be advisable to define additional stages to group these neural activities in areas distinct from the cognitive aspects associated with stage 5. Alternately, it may be useful to define an input stage related to the limbic sensory channels and an output stage related to limbic related responses (although these may all fall within the signal definitions of stages 6-7)

The reports of Barbas & Zikopoulos relating to the emotional aspects of the PFC appear to offer information on extending this diagram (pages 80-81). Similarly, Gottfried et al. offer additional information related to the olfactory and gustatory inputs to the PFC (Section 11.7.9 and Zald & Rauch). They suggest areas 11l and 13l are involved in olfactory cognition.

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As in other areas of the cerebral cortex, the left and right portions of the prefrontal lobe are able to operate independently. They normally coordinate via commissure⁴¹. When operating more independently than desired they can become the source of serious disease that in the past have led to prefrontal lobotomies designed to sever these commissure.

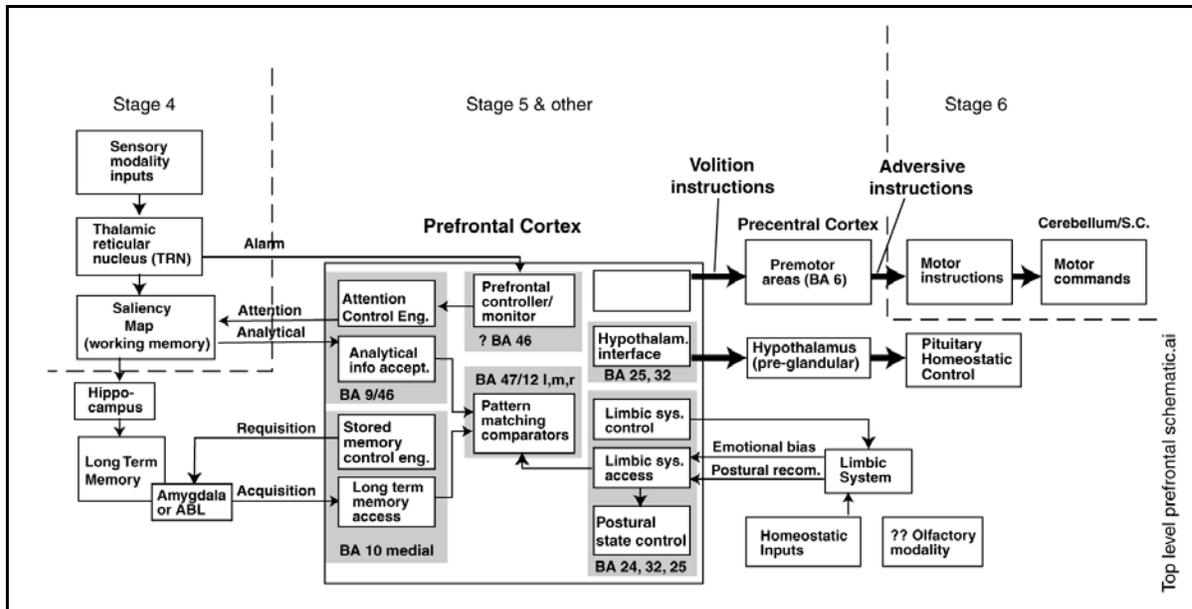


Figure 12.2.1-2 Candidate top level block diagram of prefrontal cortex with cytoarchitecture overlay ADD. While stages 4 & 6 are clearly delineated, stage 5 is subject to further subdivision. A clear role and location for the major prefrontal cortex element associated with the “mind” and issuing volition instructions to the premotor areas has yet to be isolated. See text.

It is very likely that the executive contains a master controller (labeled the prefrontal controller in this figure) that is capable of choosing the mode of operation of the executive. This function is the source of the mind’s ability to act spontaneously, its “volition.” This controller is proposed to be in contact with all of the individual engines within the prefrontal cortex directly associated with the executive; it would be in contact with engines not yet defined in this figure..

It is highly likely the operation of the prefrontal controller of the executive is highly responsive to any alarm mode signal received from the TRN. If true, this response to an alarm signal provides a logical starting point for the analysis of the operation of the executive. **Section 4.2.4** defines a series of operating modes within the sensory modalities of the neural system. It is likely a similar set of operating modes is found within the executive of the prefrontal cortex.

Initially, it is clear the executive lacks a sophisticated computational capability. This means no transcendental calculations in accordance with the rest of the system. It also means the executive relies primarily on pattern matching; it probably can perform pattern matching on multiple reference patterns in parallel. The reference patterns may represent memories that are parallel in relative time or the memories may consist of a series of patterns that are sequential in character. See **Section 12.2.3**.

⁴¹Thottakkara, P. Lazar, M. Johnson, S. & Alexander, A. (2006) Applications of Brodmann’s area templates for ROI selection in white matter tractography studies *Neuroimage* vol 29(3), pp 868-878

Ungerleider and associates have provided a simpler version of the above figure⁴². It focused on only the visual pathways leading to the prefrontal cortex from a variety of areas based mostly on traffic analysis related to the cerebrum. It did not address the role of the thalamus as a supervisory or switching point.

12.2.1 The supervisory function within the executive

Shallice has described the primary mechanism within the prefrontal lobe as an "executive" with supervisory powers⁴³. He has also proposed that this executive is "fractionated" into subsidiary mechanisms. Shallice stated in his 1996 conclusion, "Clearly this has been a very preliminary discussion." Within the constraints discussed in the next section, his proposals appear compatible with the above initial figure and the remainder of this work. It might be said we are addressing the issue from different perspectives.

Shallice discussed his concepts of supervisory control in the prefrontal lobe further in 2004⁴⁴. His abstract begins, "Three different frameworks for understanding the functions of different regions of prefrontal cortex—working memory, general intelligence, the Supervisory System approach—are compared." The text includes much valuable and specific information. He notes:

- Dramatic evidence that area 9/46 is involved in operations rather than storage per se.
- Working memory was associated with bilateral activities of Brodmann's area (BA) 8 and the parietal lobe.
- Preliminary evidence that the "seat of general intelligence, *g*," is located in the lateral prefrontal cortex.
- A proposed two-level Supervisory System that includes a lower level system of action and thought selection—known as contention scheduling. "Contention scheduling implements routine actions."
- Bilateral damage to the frontopolar regions, BA 10 & 11 leads to "severe impairment of 'intention marker' realization." The intention marker is highly conceptual in the text.

His figure 68.3 suggests the same mode of operation as in the above figure but in somewhat less detail. His figure 68.4 offers more conceptual features but less specific definition. It is adopted from Shallice & Burgess, 1996. The "intention marker" is conceptualized by a single off-the-main-path box.

12.2.2 Limits on psychological concepts of prefrontal lobe operations

A wide range of papers have appeared from the psychological community that use examples, first or second person, to develop concepts of prefrontal lobe operation. The great majority of the examples used in the literature, such as the Hayling sentence completion test, involve signal processing external to the prefrontal lobe. As shown in this work, using spoken or written sentences under the assumption that each word of the text is processed by the prefrontal lobe is unrealistic. Routine reading, walking and many other major functions rely upon subroutines implemented at lower levels within the brain and only supervised by the executive function of the prefrontal lobe. This supervision involves the receipt of high level cognits and the issuance of high level adversive instructions.

The psychology community has even defined what they describe as tasks that load the prefrontal lobe maximally. They have then described differential experiments where one task loads the system heavily and the other does not. These are entirely conceptual situations

⁴²Ungerleider, L. (1995) Functional brain imaging studies of cortical mechanisms for memory *Science* vol 270, pp 769-775

⁴³Shallice, T. (1996) The domain of supervisory processes and temporal organization of behavior *Phil Trans R Soc Lond B* vol 351, pp 1405-1412

⁴⁴Shallice, T. (2004) The fractionation of supervisory control *In Gazzaniga, M. ed. The Cognitive Neurosciences*, 3rd Ed. Cambridge, MA: MIT Press Chap. 68

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with little to no evidence of appropriateness. Shallice has described the tasks in a useful experiment.

“The range of performance of normal subjects must leave an ample region in which to observe clearly impaired performance. Normal performance must be approximately stationary, and theoretically interesting variations on the basic task must be effectively usable on the individual subject. These three conditions are frequently not all satisfied with tasks that load heavily on ‘frontal functions’ ”

He offers no concrete test to determine what tasks meet his requirements.

The goal of all psychological investigations at this time should be to explore the fundamental mode of prefrontal lobe operation in order to understand more complex modes in the future. To explore this mode, the protocol must provide a stimulus whose cognit is reasonably well understood and seek to observe outputs of the system that represent neural signals as similar to the aversive instruction of the frontal lobe as possible.

A candidate stimulus exciting the fundamental mode of frontal lobe operation might be the full face view of a carnivore larger than the subject approaching the subject rapidly with teeth and fangs exposed. This stimulus should cause a very primitive response that does not rely upon training, does not employ any complex analytical routines and result in one or more actions associated with a flight response.

The full face view is needed so the subject knows the carnivore is stereoscopically ranging on the subject. The size of the stimulus defines one aspect of the threat. The approaching velocity of the stimulus further defines the threat.

The visual stimulus must be presented at the point of fixation. Otherwise, the pointing subroutines associated with the alarm mode of vision must be considered in the overall data reduction plan (**Section xxx**).

12.2.3 Long term memory access & utilization

Wagner et al⁴⁵. also explored the role of the prefrontal cortex and memory. They specifically address the questions associated with the lower left corner of the prefrontal cortex block in the previous figure. Their first action is to divide the process of memory retrieval into multiple steps. They speak of the generation of a search requisition, the initiation of a search requisition, the recovery (acquisition) of information from episodic memory, the representation of retrieval cues and products in working memory, and the evaluation of the relevance of the acquired information to the current task goal.. They associate these individual tasks with the right anterior prefrontal cortex at or near BA 10 (the medial network of Ongur et al.) and the dorsolateral prefrontal cortex at or near BA 46 and 9 (near BA 10r of Ongur et al.). They suggest the function is primarily right lateralized, although reports of left lateralization are common. They also suggest these functions are not restricted to episodic memory. The sequential nature of these steps is emphasized when they note that the evaluation of the acquired memory is impossible if requisition and subsequent acquisition has been unsuccessful. Overall, their experiments did not give definitive results using their specific tests.

Their assertion that their measurements were right lateralized may be due to the fact they used only right-handed subjects.

The term “standard tests” is showing up frequently in the literature in attempts to define the role of the prefrontal lobe. However, little to no justification for these standard tests being the appropriate tests has been found in the literature. How the tests have risen to the level of a standard is also difficult to determine.

⁴⁵Wagner, A. Desmond, J. Glover, G. & Gabrieli, J. (1998) Prefrontal cortex and recognition: Functional MRI evidence for context-dependent retrieval processes Brain vol 121, pp 1985-2002

In a second paper, Wagner et al. have provided a review of the role of the parietal lobe with respect to episodic memory⁴⁶. [xxx expand]

Brand & Markowitsch discuss LTM retrieval⁴⁷. "In the context of memory retrieval the connections between the anterior temporal pole and the OFC via the ventral branch of the uncinate fascicle are of crucial interest. This regional combination in the right hemisphere triggers the retrieval of episodic events, while the one in the left hemisphere primarily triggers retrieving facts (with citations)." They provide a conceptual level block diagram of their suggested retrieval system (page 289).

Baxter et al. have provided valuable data on the requirement that at least the basolateral portion of the amygdala (ABL) and the OFC must operate in series to recall long term memory.

12.2.3.1 Connections to the limbic system

The limbic system is difficult to define. It can be described anatomically as the limbic lobe. However, this does not appear to be a meaningful functional definition. The limbic system is generally considered to include the amygdala, the hypothalamus, the hippocampal formation and several other minor anatomical elements. Some investigators include the thalamus and the olfactory sensory modality in the limbic system. This work does not include the thalamus in the limbic system because of its critically important switching, control and non-declaratory memory functions. The primary focus of the limbic system shall be considered its emotional, visceral and homeostatic responsibilities. While the olfactory modality does not appear to belong to the limbic system functionally, its very close anatomical association cannot be easily dismissed.

Functionally, the amygdala has been implicated in long term memory storage and recall. This role is not normally associated with the limbic system. Roesch & Schoenbaum⁴⁸ have provided a broad discussion of the interface between the basolateral amygdala (ABL) and the OFC and have noted the findings of Baxter et al⁴⁹. Baxter et al. demonstrated conclusively in carefully developed behavioral test protocols that the OFC and ABL must operate in series to support the utilization of long term memory.

Price and colleagues have provided considerable traffic analysis related to the prefrontal lobe of monkeys. They have shown extensive connections between the amygdala, as well

⁴⁶Wagner, A. Shannon, B. Kahn, I. & Buckner, R. (2005) Parietal lobe contributions to episodic memory retrieval *Trends Cog Sci* Vol 9(9), pp 445-453

⁴⁷Brand, M. & Markowitsch, H. (2006) Memory processes and the orbitofrontal cortex In Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press. Chapter 11

⁴⁸Roesch, M. & Schoenbaum, G. (2006) From associations to expectancies: orbitofrontal cortex as gateway between the limbic system and representational memory In Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press. Chapter 8

⁴⁹Baxter, M. Parker, A. Lindner, C. et al. (2000) Control of response selection by reinforcer value requires interaction of amygdala and OFC *J Neurosci* vol. 20, pp 4311-4319

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as other elements of the limbic system, and the medial network of the lobe^{50,51,52}. These connections are indicated conceptually in the lower right corner of the candidate top level prefrontal lobe schematic. The symbol BA *** is used to reflect the broad level of interconnections of the limbic system with areas 11m, 13a, 13b, 14c and 14r (the interface network of Ongur), as well as 25, 32 & 24 (the medial network of Ongur), suggested on page 46 of the 2006 paper. An expanded version of this part of the figure will probably be needed to delineate the individual areas of the prefrontal lobe and the limbic system as additional stimulus related signal paths are identified.

The roles of the amygdala and the hypothalamus are quite different.

Fuster (4th ed, page 199) has described BA 24 as the crossroads of pathways linking the limbic system to the prefrontal cortex. He defines BA 24 and 32 as forming the anterior cingulate cortex, with a significant role in emotional performance.

12.2.3.2 Memory retrieval processing in humans

Rugg has recently discussed and differentiated between the use of fMRI and event-related potential (ERP) techniques in studies of memory retrieval. They note the limited time resolution and sub-centimeter but super-millimeter spatial resolution of fMRI compared to the higher temporal resolution but poorer spatial resolution of the ERP technique. The work does not seem to differentiate between the location of stored memory and the potential location of the prefrontal engines associated with memory retrieval in the top level block diagram of the prefrontal cortex. Rugg does not identify the areas of his responses other than as the right dorsolateral region of the prefrontal cortex. This area could be described as one of the 47/12 areas of Ongur and others.

12.2.4 Control of the homeostasis of the subject

Price has described the interconnection of the prefrontal cortex with both the thalamus and the hypothalamus, the gateway to the glandular system⁵³. He indicates the complexity of the connections to the thalamus and beyond are currently undescrivable. Significant nerves connect to both the orbital and medial networks of the OFC. He also describes the significant volume of neurons proceeding to the hypothalamus from BA 25, BA 32 & the caudolateral orbital areas 1a1 and 12o in the macaque monkey..

12.2.5 Characteristics of the pattern matching comparators

The pattern matching comparators of stage 5 are likely to share many properties with the comparators found within the lateral geniculate nucleus (LGN) of stage 4. They both compare multi-bit (using the term loosely in the analog mode) signals from multiple sources in order to ascertain similarities and differences between the two packets of information. The LGN is formed by multiple folds of the cortex within a very small area (**Section 15.6.6** of "[Processes in Biological Vision](#)"). [xxx better example of folding in earlier chapters.] Each fold exhibits a visuo-topic rendition of one signal channel representing the external scene. Within

⁵⁰Carmicheal, S. & Price, J. (1995) Limbic connections of the orbital and medial prefrontal cortex in macaque monkeys *J Com Neurol* vol 363, pp 615-641

⁵¹Carmicheal, S. & Price, J. (1996) Connectional networks within the orbital and medial prefrontal cortex of macaque monkeys *J Comp Neurol* vol 371, pp 179-207

⁵²Price, J. (2006) Connections of orbital cortex *In Zald, D. & Rauch, S. eds. The Orbitofrontal Cortex. Oxford: Oxford Univ Press. Chapter 3*

⁵³Price, J. (2006) Connections of orbital cortex *In Zald, D. & Rauch, S. eds. The Orbitofrontal Cortex. Oxford: Oxford Univ Press Chap 3.*

that fold, the input from the left and right eyes are compared. Each fold exhibits two layers with heavy myelination suggesting these layers are populated by many stage 3 axons terminating in these layers. The table in [Figure 12.1.2-4] would suggest, areas 47/12l, 47/12m and 47/12r are likely regions for these comparators. Although these areas are not generally described as striated or reticulated as are the LGN's, they do exhibit pairs of Baillarger's Bands (layers of heavy myelination running parallel to the pia matter, Section xxx). The intervening layer can accommodate a large number of small comparator neurons synapsing with the axons terminating in the Baillarger Bands.

Based on the fact pairs of Baillarger's Bands are only reported in areas 47/12l, 47/12m & 47/12r, it is proposed that these areas contain the pattern matching comparators of the prefrontal lobe. These areas are the primary elements of the orbital network defined by Ongur et al.

12.2.6 Confirmation of the top level block diagram

As suggested earlier, the design of the test protocol is critical to determining the functional significance of different PFC areas. The earliest fMRI experiments during the 1990's defined protocols based on conventional theories from psychology that were not highly correlated with the way the brain actually functions.

Henson, Shallice & Dolan⁵⁴ performed an early set of fMRI tests using the BOLD technique to verify the monitoring hypothesis of Burgess & Shallice, 1996. Their paper is an excellent example of exploratory research in a new area of considerable complexity. They used only right-hand subjects and focused on using printed words (larger than the field of the foveola) as stimuli. The underlying assumption was the literal form of the words were analyzed within the PFC (which is not supported by this work). The paper raised more new questions than it answered. Their conclusion section was a single very brief paragraph. It provided only a preliminary claim that the major "monitoring" function within the PFC is located within BA 46 (as delineated in the above figure).

Braver et al. have provided a comprehensive study of the prefrontal cortex based on a series of carefully defined test protocols⁵⁵. They used only right-handed subjects. They undertook tests to demonstrate task-selective operation and material-selective operation. The results are extensive and sophisticated with comparisons to a variety of proposed models. They provided both color fMRI images (T=1.5) and coordinates using the Talairach & Tournoux system. They suggest the separation of the PFC areas involved in working memory and long term memory as depicted by the shading in the above figure. They also claim to have located a bilateral difference wherein the word-specific regions located preferentially in the left hemisphere and face-specific regions located preferentially in the right hemisphere. Their task-specific experiments did not support their hypothesis that the frontopolar prefrontal cortex (FP-PFC) was task selective. Their work opened up a variety of new experimental paths yet to be reported.

Fuster (4th, page 371) has described and reviewed the literature of two distinct types of models of the PFC; the modular type and the network type. The distinction between the two appears to be more semantic than physiological. Recent fMRI activity appears to support the network type more strongly as the resolution of the MRI hardware increases.

12.2.7 The search for the executive, the critical element of the mind

The above figure provides a rational delineation of the prefrontal cortex into a range of functional engines. However, the literature says little about the traffic from the PFC to the premotor areas and very little about BA 46 or the precentral opercular area, the PrCO.

⁵⁴Henson, R. Shallice, T. & Dolan, R. (1999) Right prefrontal cortex and episodic memory retrieval: a functional MRI test of the monitoring hypothesis *Brain* vol. 122, pp 1367-1381

⁵⁵Braver, T. Barch, D. Kelley, W. et al. (2001) Direct comparison of prefrontal cortex regions engaged by working and long term memory tasks *NeuroImage* vol 14, pp 48-59

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Barbas & Zikopoulos have described the interconnections between the lateral prefrontal areas, including BA 46 and the frontal eye areas of BA 8⁵⁶. They also note, "Among prefrontal areas, posterior lateral area 8 and caudal area 46, the areas that have connections with early-processing sensory areas, also have the strongest connections with the neighboring premotor areas."

It is plausible that BA 46 includes the executive because of its association with the prefrontal controller/monitor and the attention control engine of the above figure.

A potential problem in isolating the executive within the PFC is the fact that most of the current imaging techniques rely upon differential imaging, seeking a change in nuclear chemistry as a function of brain activity. If the executive operates as a constant activity level engine, these differential techniques will be ineffective in locating it. It is rational to think of the executive as a constant activity engine except during periods of deep anesthesia.

Even if the executive should occupy only a fraction of BA 46, it would still constitute several million individual neurons (a complexity similar to a Pentium IV microchip). If the executive operates at a fixed energy consumption level, it could be described as a syncytium from both a morphological and physiological perspective.

A constant activity level executive might help explain the ability of the mind to jump to apparently random thought processes at apparently random times. In the absence of attentive activity, the output of the mind would occasionally generate output patterns that were similar to or identical to the acquisition commands for retrieval of specific LTM patterns.

12.3 Perception as both a tool and interference in cognition

Understanding the deterministic mechanisms of cognition is frequently difficult because of the large number of anecdotal situations that must be accommodated.

12.3.1 A surprising problem in navigation

Girdhar & Dudek have presented a chapter on navigation in the context of both biological and robotic systems⁵⁷. It is worthy of review. **Figure 12.3.1-1** reproduces their figure 11.2. It can be interpreted from either a robotic or biological perspective.

⁵⁶Barbas, H. & Zikopoulos, B. (2006) Sequential and parallel circuits for emotional processing in primate orbitofrontal cortex *In* Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press pp 57-83

⁵⁷Girdhar, Y. & Dudek, G. (2011) A surprising problem in navigation *In* Harris, L. & Jenkin, M. eds. *Vision in 3D Environments*. NY: Cambridge Univ Press Chap 11

In either case, the online condition can be considered as operating in real time and the offline as operating in a period of reflection. In their lexicon, a navigation summary consists of a group of images, both recently acquired and from memory being assembled into one set of images that describes the relevant object(s) from a range of perspectives.

They provide a more detailed caption to this figure:

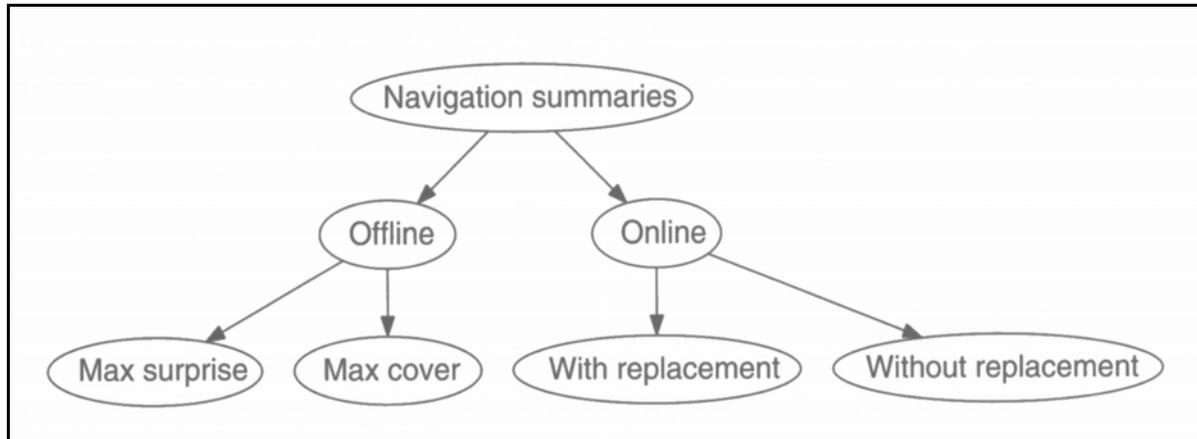


Figure 12.3.1-1 Navigation summaries can be generated offline or online. From Girdhar & Dudek, 2011.

“Offline, we can focus either on picking images which are the most surprising or on picking images which describe the maximum number of observations (maximum cover). Online, we can either make our image choices irrevocable or allow them to be replaced by a more suitable image from a future observation.”

In the context of a biological system, questions are raised as to how much of this process is performed via declaratory and how much via non-declaratory memory. Similarly, how much of the processing is controlled by the executive level of cognition (the TRN) and how much is controlled by the declaratory level associated with attention (the Prefrontal cortex). The goal of this information extraction (stage 4) and cognition (stage 5) operation is to achieve a set of images which minimizes *surprise* in the observation of the world. Worded differently, the goal is to prepare a set of images that insures one can recognize grandma (or falsify an image as not that of grandma), from any angle and in any context. In a larger context, the image set can represent any scene, of any complexity.

Their section 11.3 attempts to define what they call a *Bayesian surprise*. Using set theory, they attempt to define the level of difference between the previously stored navigation summary and a new input. They use a modification of Shannon’s basic equation of information content for this purpose.

They develop a set of strategies based on their implementation of set theory, including a “Wobegon strategy,” from Garrison Keeler’s famous line about Lake Wobegon, “where *all* of the children are above average.”

As in the usual situation, much of this type of operation is carried out in the non-declaratory arena of biology unless a serious conflict arises in which case the declaratory elements are called upon to make a decision, or call for more observations of the scene.

The navigation summaries may well be the actual image sets (in the generic sense of images, smells, touch sensation patterns, etc.) that are stored in the saliency map.

Epstein & Macevoy provide a discussion in chapter 12 of the same book of where the navigation summaries might be stored. Some of their assertions show a lack of familiarity of

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earlier work in this area based on lesions to the cortex. On the other hand they did identify a particular region of the hippocampus, "labeled the parahippocampal place area (PPA) because it responds preferentially to images of places (i.e., scenes)." Unfortunately, they are unable to define what "a place (i.e., a scene)" is. Their discussion only scratched the surface in this area.

12.3.2 Many perceptions play a major role in cognition

Rock has updated an earlier publication focused on the apparently misleading perceptions associated with human vision⁵⁸. However, many of these perceptions may be used constructively in extracting information from a scene. This appears to be particularly true in the context of stereopsis. The book includes hundreds of perceptions and misperceptions. The examples suggest the importance of prior learning in the interpretation of many scenes.

12.4 Potential functional role of Baillarger's bands EMPTY

The inner and outer bands of Baillarger are generally associated with areas of striated cortex, not only in the cerebral cortex but also in the engines of the diencephalon. In those areas, the striated cortex is generally associated with arrays of neurons with long neurites employed in the correlation function. It is proposed these bands play a similar role in the prefrontal cortex.

Baillarger's inner band is typically recognized in layer IVb of cortical tissue with the outer band typically in band V. Ongur et al. however recognize Baillarger's inner band in layer III.

It is critically important to note the stain used on the neural tissue if observation of Baillarger's band is to be optimum.

12.5 Major neural paths to/from the prefrontal lobe

McFarland & Haber have provided a comprehensive paper on the morphology of portions of the cerebral cortex and their interpretation of the connections associated with the PFC involving elements of the thalamus and the motor modality. Their summary figure was presented in **Section 11.8.2**. It excludes many of the more detailed relationships incorporated in the later versions of Fuster that more closely parallel the hypothesis of this work. Most significantly the figure contains the label thalamus when the text and caption describe this entity as the thalamic reticular nucleus (TRN). Their proposed organization of the signal paths between the TRN, the basal ganglia and multiple areas of the PFC of twenty adult macaque monkeys (*Macaca nemestrina*) is worthy of close examination.

Fuster has provided his view of the major connections to the prefrontal cortex⁵⁹. He has provided one schematic associated with motor functions and one associated with emotional functions. The motor figure lacks clarity because it does not separate the sensory related elements from the true motor related elements of the brain. This is a common problem in the psychology literature. **Figure 12.5.1-1** shows an alternate figure to his figure 2.16 that addresses this issue. It separates the afferent sensory signal paths (shown on the left) from the efferent signal paths (shown on the right). It also focuses on the forward (or information carrying, fundamental) flow of information, and largely omits the potential backflow of status related command and control signals. Virtually all of the paths shown contain a reverse or backflow component. These presumably carry supervisory signals confirming signal or

⁵⁸Rock, I. ((1995) Perception. NY: Scientific American Library

⁵⁹Fuster, J. (2008) The Prefrontal Cortex, 4th Ed. NY: Academic Press page 41

information receipt in good order. In some cases, the return signals (such as those from the occipital lobe) go to a different portion of the diencephalon (in this case the TRN) than where the forward signals originate (in the LGN).

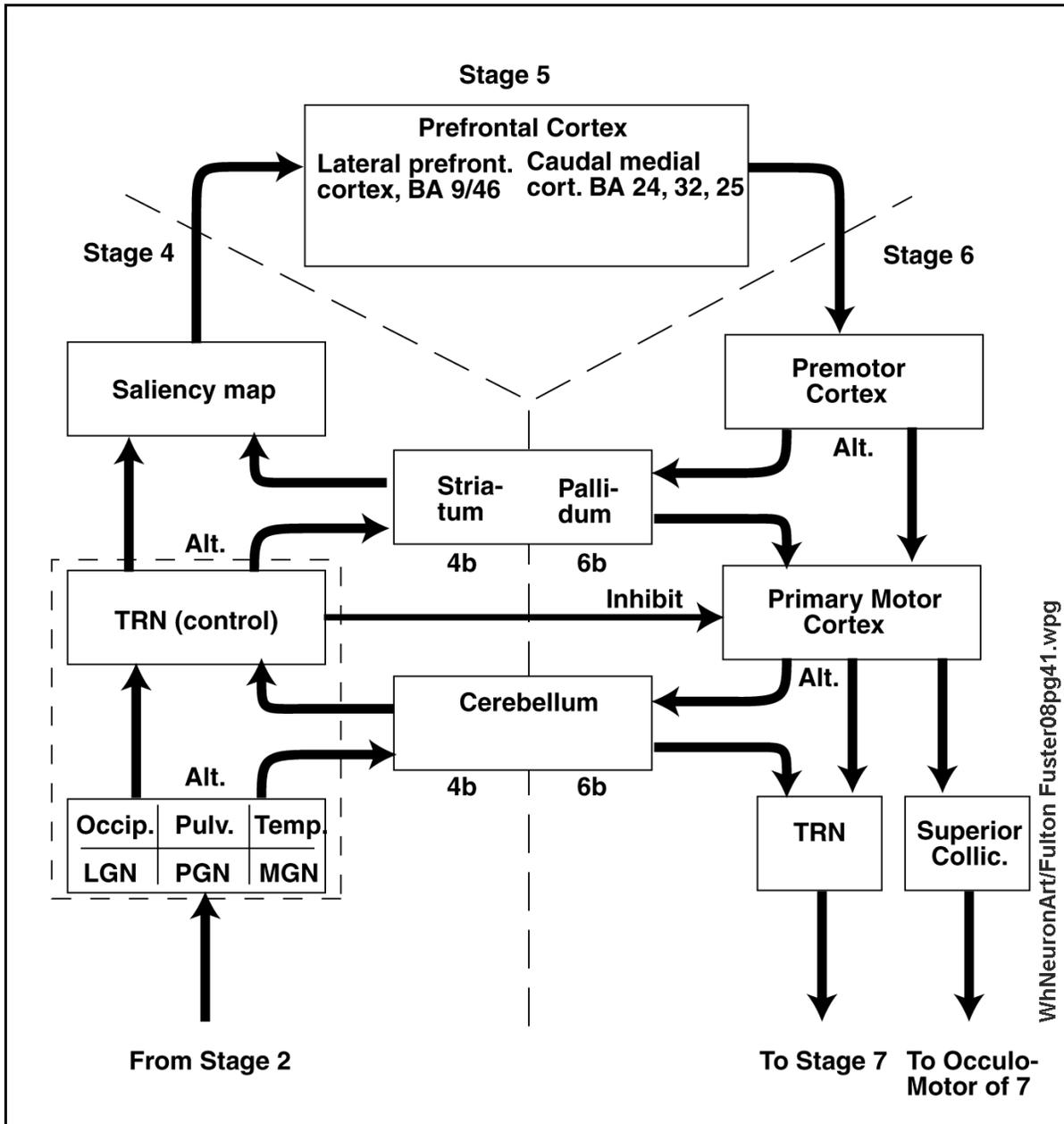


Figure 12.5.1-1 Traffic flow to and from the prefrontal cortex related to the motor function. The afferent stage 4 activity is shown for reference. The afferent role of the diencephalon is shown in greater detail within the dashed box (along with the occipital and temporal lobes of the posterior association cortex), but does not include chemical and somato sensory inputs. The dual roles of the cerebellum and basal ganglia are shown explicitly. Alt; alternate paths taken under the supervisory control of the TRN. See text. Compare to Fuster, 2008, pg 41.

The prefrontal cortex is described in terms defined in **Section 12.2**. However, some of the assignments within the prefrontal cortex remain tentative. The morphological terminology

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related to the prefrontal cortex remains confused in the literature (LeDoux, 2007). Price, writing in Zald & Rauch, assert the amygdala connects primarily to BA 24, 32, 25 & portions of 14 (at least in the monkey). Barbas & Zikopoulos, also writing in Zald & Rauch, provide a series of conceptual block diagrams of connections to the orbitofrontal cortex apparently based primarily on traffic analysis.

Stage 4 briefly illustrates the operation of the visual and auditory channels (LGN, PGN & MGN, etc.) in lieu of showing all the sensory input channels.

The TRN plays a significant supervisory and control function related to the motor system. It inhibits motor action during sleep and other special situations. In conformity with its switching and control function, the TRN influence on the motor system is inhibitory rather than graded. The figure replaces "midbrain pons" of Funster with the more definitive superior colliculus and hypophysis. It also shows the outputs of the superior colliculus projecting to the stage 7 neuro-affectors. the hypophysis (pituitary gland) is the major transition element between the neural system and the glandular system.

The dual roles of the cerebellum and the basal ganglia are emphasized in this figure. Both appear to have elements that are associated with the afferent sensory system (labeled stage 4b) and the efferent motor system (labeled stage 6b). The close cooperation of the two halves of each element becomes most clear during training of the subject. The cooperation is especially important during training for a new motor task that involves visual or acoustic sensory information if optimum results are to be achieved.

The term alternate appears at several points in the figure. It indicates a choice can be made between a direct path and a circuitous path through a portion of the cerebellum or basal ganglia. For simple activities, or alarm mode operations, the direct forward signaling path can be taken. This path may result in a clumsy motor response but it may be necessary during alarm mode operations. In a young child, the direct path is a precursor to starting the learning process. For learning, and especially of more complex operating activities, it may be necessary to use the circuitous path. Initially, the circuitous path is used to learn a new sensory response profile or to learn a new complex motor activity. It is clear the two halves of the cerebellum coordinate their signaling states during the process of a learning episode.

The figure includes an explicit saliency map describing the environment of the subject. This saliency map is believed to be stored in the yet undefined short term memory facility of the neural system. There are opposing proposals in the literature. Some suggest both short term memory and long term memory are initially stored in the hippocampus, with selected short term memories made permanent under instructions from the prefrontal cortex. Others suggest a separate short term memory wherein its contents are transferred to long term memory via the hippocampus and under the instruction of the prefrontal cortex.

The role of long term memory is not shown explicitly in this figure. Long term memory is becoming closely associated with the hippocampus with access from BA 10 of the prefrontal cortex. This work has not made a determination as to whether long term memory should be considered part of the sensory (afferent) neural system, part of the cognitive system (stage 5), or part of the efferent system (stage 6). Its role may justify a separate characterization with respect to its functional area.

Damasio et al⁶⁰. have also provided a largely conceptual block diagram of the human brain focused on stages 5 and 6 and resulting primarily from one specific medical case, an individual known as EVR. They suggest the prefrontal lobe can be divided into two distinct neuroanatomic systems based on the results of their observations of the subjects response to a series of delayed response (DR) and delayed action (DA) tasks.. They do not associate particular physical areas of the prefrontal lobe with specific subordinate areas or specific

⁶⁰Damasio, A. Tranel, D. & Damasio, H. (1991) Somatic markers and the guidance of behaviour: theory and preliminary testing *In* Levin, H. Eisenberg, H. & Benton, A. eds. *Frontal Lobe Function and Dysfunction*. NY: Oxford Univ Press Chapter 11

motor functions. However, their delineation appears to be compatible with that described here and in Sections 12.1.2 & 12.2.

Figure 12.5.1-2 shows an alternate to Funster's figure 2.17 describing the connectivity of the prefrontal cortex with structures involved in emotion. Funster's figure lacks any focus. While one output is shown conceptually, no input, or initial act of volition, is shown. All signal paths are shown as bidirectional (except one via the cingulate cortex and the conceptual output) but without further comment.

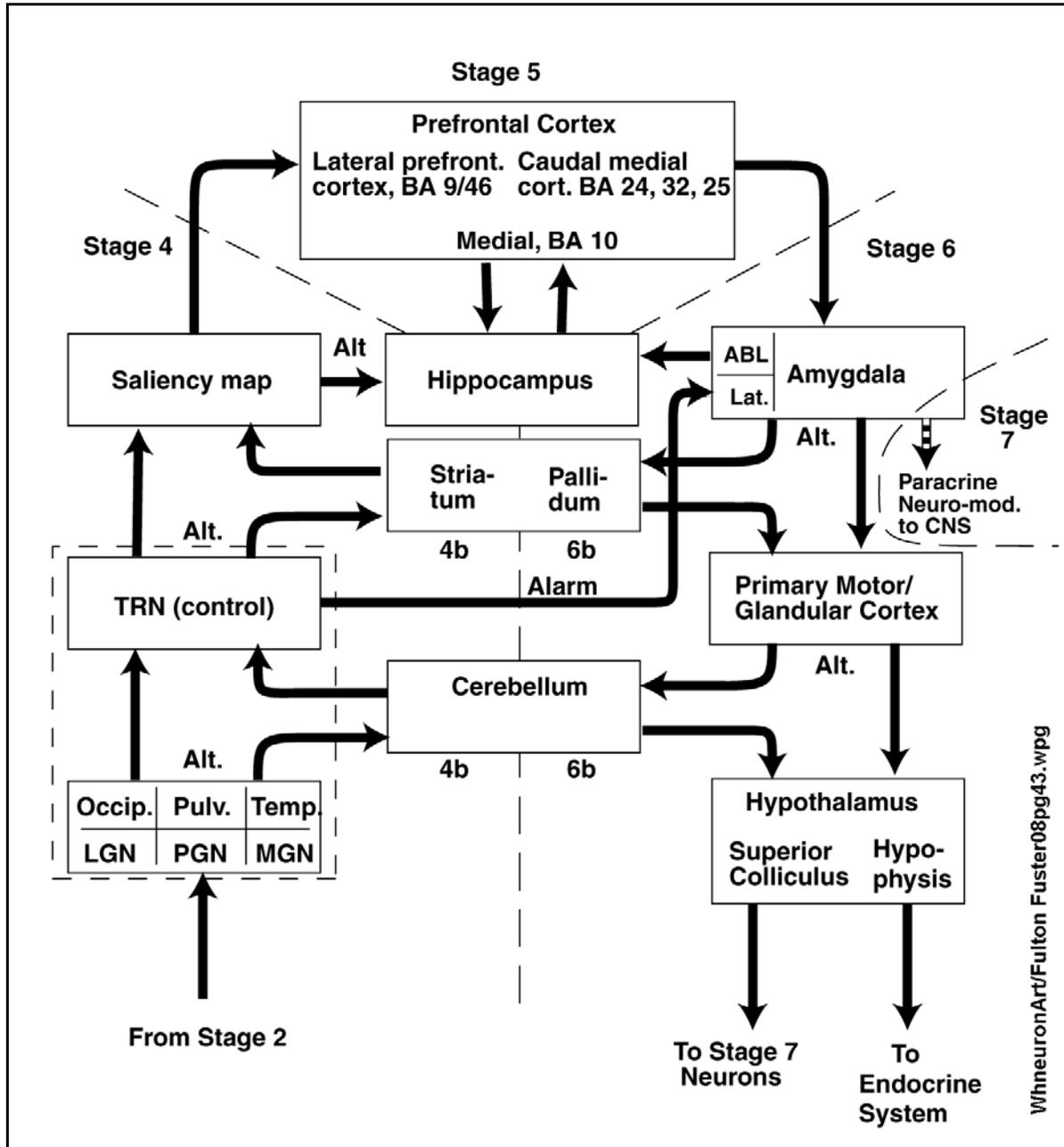


Figure 12.5.1-2 Connectivity of the prefrontal cortex with structures involved in emotion. The release of neuromodulators into the CNS from the amygdala is a critical mechanism in this figure. Compare to Funster, 2008, pg 43.

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In this figure, only the fundamental forward paths of the neural system are shown. Many of these paths include reciprocal signal paths. Many supervisory and control paths also emanate from the prefrontal cortex and the thalamic reticular nucleus (TRN). Stage 4 briefly illustrates the operation of the visual and auditory channels (LGN, PGN & MGN, etc.) in lieu of showing all the sensory input channels. The prefrontal cortex is again described in terms defined in **Section 12.2**. However, some of the assignments within the prefrontal cortex remain tentative. The morphological terminology related to the prefrontal cortex remains confused in the literature (LeDoux, 2007). Price, writing in Zald & Rauch, assert the amygdala connects primarily to BA 24, 32, 25 & portions of 14 (at least in the monkey). The hippocampus, amygdala and hypothalamus constitute the major commonly defined elements of the limbic system. It is the limbic system that is usually associated with the emotional aspects of the brain.

Fuster describes the

The cingulate cortex shown in the Fuster picture is not illustrated here because of its poorly defined functional character. The posterior association cortex of Fuster is represented by the occipital lobe and temporal lobe within stage 4 of the figure.

Speaking from the perspective of neuroanatomy, Freese & Amaral note in 2009, "There is virtually no available information on the connectivity of the human amygdala⁶¹." However, from the neurophysiological perspective, there is considerable information. They proceed to provide a very conceptual first order graphic of these connections on page 16. Continuing, Freese & Amaral discuss the intra-amygdala connections on page 10, "In the primate, the lateral nucleus (of the amygdala) projects to all other nuclei of the amygdaloid complex, although the projections vary in magnitude." "Projection to all" implies first order traffic analysis, "although variance in magnitude" is a conclusion from second order traffic analysis. The figure shown is reoriented from Fuster to separate the afferent from the efferent functions. The major changes are the addition of the neuro hormonal system to the relationships and the realization that the hormonal system exhibits both paracrine components within the CNS itself and exocrine components feeding the fluid channels of the body including the PNS. There is no functional means to separate the primary motor and primary glandular cortex. The primary motor aspects of the cortex have just been evaluated more thoroughly.

LeDoux also noted the recent interest in the amygdala in a solicited primer⁶². He also noted the fact the amygdala was a source of paracrine neuro-modulator release within the forebrain of the CNS, including the amygdala itself.

Speaking of the amygdala, LeDoux & Schiller note⁶³, "There are three categories of so-called 'neuromodulators', peptides, released locally from axons in the amygdala; amine transmitters, which are released widely in the brain from distal areas; and hormones, which reach the amygdala via the bloodstream. The figure shows one region of the amygdala complex containing neuro-affecter neurons (stage 7) exuding peptides into the CNS. The paracrine release of neuro-modulators within the CNS by the amygdala is a critical phenomenon not previously highlighted in the literature (excepting the above comment by LeDoux). Such neuro-modulators can affect virtually every neural element within the CNS (including at least portions of the amygdala itself). Their affect may be controlled by the presence or absence of appropriate receptor sites. LeDoux & Schiller devote one page (page 49) to the matter in 2009. This phenomenon explains, and demands that, the action of

⁶¹Freese, J. & Amaral, D. (2009) Neuroanatomy of the primate amygdala *In* Whalen, P. & Phelps, E. eds. The Human amygdala. NY: Guilford Press

⁶²LeDoux, J. (2007) The Amygdala (a primer) *Cur Biol* vol 17(20), pp R868-R874

⁶³LeDoux, J. & Schiller, D. (2009) The human amygdala *In* Whalen, P. & Phelps, E. eds. The Human amygdala. NY: Guilford

the amygdala affects a broad range of neurons (theoretically all) within the CNS. As a result, it is probably impossible to isolate the individual affects that the amygdala has on the rest of the neural system.

LeDoux & Schiller go on (page 49), " The amines norepinephrine, dopamine, serotonin and acetylcholine are all released in the amygdala and influence how excitatory and inhibitory neurons interact." Their wording is subject to various interpretations and requires clarification. They do not provide any citations providing more details concerning this question. If the word "in" can be taken to mean "by" or "by and in" as suggested in the two earlier paragraphs associated with LeDoux, then the amygdala is a major, and possibly the only recognized, source of paracrine neuro-modulators within the CNS.

Chow & Cummings have elucidated the neuromodulators associated with the amygdala in preliminary form⁶⁴. However, additional clarity is needed to differentiate between neuro-modulators released within the CNS by the amygdala complex versus neuro-modulators found in the amygdala complex.

A particular problem in isolating the affects of neuromodulator release by the amygdala is its bilateral character. Unless both amygdala are affected similarly (identically), the effect of the lesioning or other technique is difficult to identify and quantify.

The potential for positive feedback via the release of neuromodulators by the amygdala is recognized. LeDoux & Schiller note, " Once the amygdala has detected an emotional stimulus, its activity can then influence the cortical processing of that stimulus." They also note, "Techniques for exploring the neurochemistry of the human brain are in their infancy." Their pages 52-53 explore the general knowledge of the affect of the amygdala related to fear.

On page 53, LeDoux & Schiller note, "the basal nucleus, which influences instrumental behaviors and actions through connections with other forebrain regions, mostly notably the striatum." Based on this work, it is suggested the connection was with the pallidum (stage 6b) rather than the striatum (stage 4b) although the later is not excluded on factual grounds.

Quoting LeDoux & Schiller (page 44), "It is easy to be confused by the terminology used to describe the amygdala nuclei, as different sets of terms are used. This problem is especially acute with regard to the basolateral region of the amygdala." They go on to review the different systems used historically.

LeDoux & Schiller give one of the most comprehensive descriptions of the amygdala. They note, "Cells in the amygdala are known to be relatively 'silent'." They also note, "The so-called 'silence' of th amygdala observed in animals studies refers to the activity of excitatory projection neurons." The excitatory projections neurons are stage 3 neurons. The massive numbers of analog stage 6 neurons do not show any obvious changes in signal character between emotional and non-emotional periods.

The lateral nucleus is generally considered the evaluation nucleus of the amygdala. It is shown receiving the alarm mode signals from the TRN. The detailed characteristics of these late stage 4 signals are unknown. Their origin is developed in **Section 8.xxx**.

The role of the amygdala in controlling access to long term (presumably declarative) memory via the hippocampus remains speculative. Most of the experimental data is based on lesions that may have involved both bodies instead of exclusively one or the other. The challenge in identifying the elements (structures) involved in emotion is the scope of the involvement and the limited ability to isolate the contributions of individual elements. As an example, the amygdala is believed to have a significant role in controlling the recall (if not the writing) of long term memory, as well as act as a major evaluator of threats to the animal in conjunction with the alarm mode of the sensory signal manipulation activity in stage 4.

⁶⁴Chow, T. & Cummings, J. (2000) The amygdala and Alzheimer's disease *In* Aggleton, J. *ed.* The Amygdala. NY: Oxford Press Chapter 20

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Ungerleider and associates have provided a much simpler version of the prefrontal lobe relating to the above figure⁶⁵. It focused on only the visual pathways leading to the prefrontal cortex from a variety of areas based mostly on traffic analysis related to the cerebrum. It did not address the role of the thalamus as a supervisory or switching point.

- - - -

Waxham⁶⁶ has asserted without citation that "Some 80% of the dopamine in the brain is localized to the corpus striatum, which receives major input from the substantia nigra and takes part in coordination motor movements. Dopamine is also found diffusely throughout the cortex, where its specific function remains largely undefined."

Combining the LeDoux & Schiller and Waxham remarks suggests the amygdala striatum relationship is a very important one significantly affecting the emotional state of the subject through the release of dopamine by the amygdala on a non-focused basis into the milieu of the brain. The introduction of dopamine into the brain pharmacologically would also expect to affect the corpus striatum significantly.

- - - -

One observation based on behavioural activity is that the release of neuromodulators by the amygdala may cause the use of more direct motor paths (eliminating activity related to the stage 6b basal ganglia and cerebellum). Significant emotional involvement typically results in less controlled motor activity. Similarly, the direct paths in stage 4 may also be preferred under stress conditions. Eliminating the circuitous paths through stages 4b & 6b can save major fractions of a second in response times.

12.5.1 Potential operating modes within the CNS

The delivery of alarm mode signals from the thalamus to the amygdala, and probably other structures within the Prefrontal cortex suggests a comparison between the operating modes of the CNS with those previously identified within the sensory modalities. **Section 7.2.1** provides the list shown in the left in **Figure 12.5.1-3**.

The modes of operation defined within the sensory modalities appear to provide a very good foundation for those associated with the cognitive modes of stage 5. The executive typically accesses the saliency map routinely to maintain an awareness of the environment. When alerted by signals delivered from the alarm center within the thalamus, they are evaluated within the amygdala and other elements for significance. At minimal significance, they may elicit analytical activity whereas at major significance they may elicit a flight or fight response. The flight or fight response may be measured, based on prior experience, or maximum in order to preserve the organism. The analytical mode of cognition may be closely associated with the concept of attention.

IDENTIFIED SENSORY MODES	PROPOSED COGNITIVE MODES
Awareness	Awareness
Alarm	Alarm
Analytical	Analytical
Volition	Volition

Figure 12.5.1-3 A comparison of Prefrontal cortex and sensory modality operating modes.

⁶⁵Ungerleider, L. (1995) Functional brain imaging studies of cortical mechanisms for memory *Science* vol 270, pp 769-775

⁶⁶Waxham, M. (2004) Neurotransmitter receptors *In* Byrne, J. & Roberts, J. eds. From Molecules to Networks, NY: Academic Press

Attention is frequently described as both, "the ability to selectively attend to and maintain information, and inhibit irrelevant stimuli and impulses⁶⁷."

The volition mode, in the context of the sensory modalities was associated with the direction of the eyes to a point of interest without external cues. The volition mode in the context of the executive is associated with any instructions to the lower neural system to take action independent of any cues to the executive. The executive may call for such action based on the recall of memory or what might be called "independent and original thought."

12.5.2 The role of the basal ganglia

The basal ganglia have played a limited role in previous discussions of the functional aspects of the human brain. The label basal ganglia appears to be a catchall for neural elements whose purposes have been poorly understood.

Hawkins made an interesting observation (page 168) relative to the large brain structures, the basal ganglia, the cerebellum and the hippocampus, that lie under the cerebral cortex and communicate with it. "All three existed prior to the neocortex. With a very broad brush, we can say that the basal ganglia were the primitive motor system, the cerebellum learned precise timing relationships of events, and the hippocampus stored memories of specific events and places."

Kenneally, writing in a popular book on language takes a different perspective⁶⁸. Quoting Lieberman, she suggests the basal ganglia play a major role in the timing of motor activity associated with language. The views of Hawkins and Kenneally may point toward the separation in neural function between speech and singing.

The difficulty of probing the basal ganglia undoubtedly contribute to this problem. The basal ganglia lie internal to, and largely below, the shell formed by the cerebrum. They include⁶⁹:

- The (neo)striatum– including the caudate nucleus (Cd) and the putamen (Put) which are similar but separated primarily by the internal capsule.
- The globus pallidus (GP)– separating anatomically into the external pallidus (Pge) and the internal pallidus (Gpi). Many works use the description pallidum for the GP.
- The subthalamic nucleus (ST)
- The substantia nigra (SN)– divided into the pars reticulata (Snr) and pars compacta (Snc). The latter is heavily pigmented and gives the substantia nigra its name.

There are other elements frequently associated with this complex or with the limbic system.

As Anderson notes, "The basal ganglia, like the cerebellum, exert profound influences on movement. Unlike the cerebellum, however, the basal ganglia receive no direct input from primary sensory systems; information used by the basal ganglia is derived primarily from the cerebral cortex." The conclusion can be drawn that the basal ganglia play a major role in stage 6 signal manipulation. **Section 11.8** describes the functional role of the basal ganglia in greater detail. They accept signals from primarily the prefrontal lobe of the cerebral cortex and contribute to the generation of premotor or motor commands prior to their propagation to the muscles. The function of the pallidum has been associated with a stage 6b in **Section 11.8**. Similarly, the elements of the striatum have been associated with stage 4b.

Baars & Gage have given a recent review of the basal ganglia that is in good agreement with the above material. While they describe the basal ganglia as the "hub" connecting the

⁶⁷Hooker, C. & Knight, R. (2006) The role of lateral orbitofrontal cortex in the inhibitory control of emotion *In* Zald, D. & Rauch, S. eds. *The Orbitofrontal Cortex*. Oxford: Oxford Univ Press Chapter 12

⁶⁸Kenneally, C. (2007) *The First Word*. NY: Penguin Group page 78

⁶⁹Anderson, M. (1989) The basal ganglia *In* Patton, H. Fuchs, A. et al. eds. *Textbook of Physiology*, 21st Ed, Vol. 1. Philadelphia, PA: Saunders Chap 30

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cognitive stage and the motor system (**Section 12.1**), this work separates the individual ganglia into distinct and important roles within stage 6 of the neural system.

12.5.3 Major neural paths of the macaque monkey

Ongur, An & Price have provided extensive and detailed information on the neural connections between the frontal lobe and the hypothalamus in the macaque monkey⁷⁰. The studies focused on paths between the orbital and medial prefrontal cortex (OMPFC), areas labeled BA 25, BA 32 and the caudolateral orbital areas lai and 12o, to the hypothalamus and related regions of the diencephalon and midbrain. [xxx expand]

12.5.4 Major neural paths of the human motor system

Many maps have been provided to describe the motor system of human. Each has been based on a different perspective. **Figure 12.5.4-1** attempts to provide a very top level block diagram combined with a map of the motor region (BA 4) of the cerebral cortex and the known responses from stimulation of these areas. This description allows for a straight forward discussion of the details of the motor system (See also **Section 19.3**). The mapping of the motor area of the cerebral cortex is the work of Penfield & Rasmussen⁷¹. The overall figure is based on concepts developed in procedural learning experiments.

⁷⁰Ongur, D. An, X. & Price, J. (1998) Prefrontal cortical projections to the hypothalamus in macaque monkeys J Comp Neurology vol 401, pp 480–505

⁷¹Penfield, W. & Rasmussen, T (1950) The Cerebral Cortex of Man: A clinical study of localization of function. NY: Macmillan

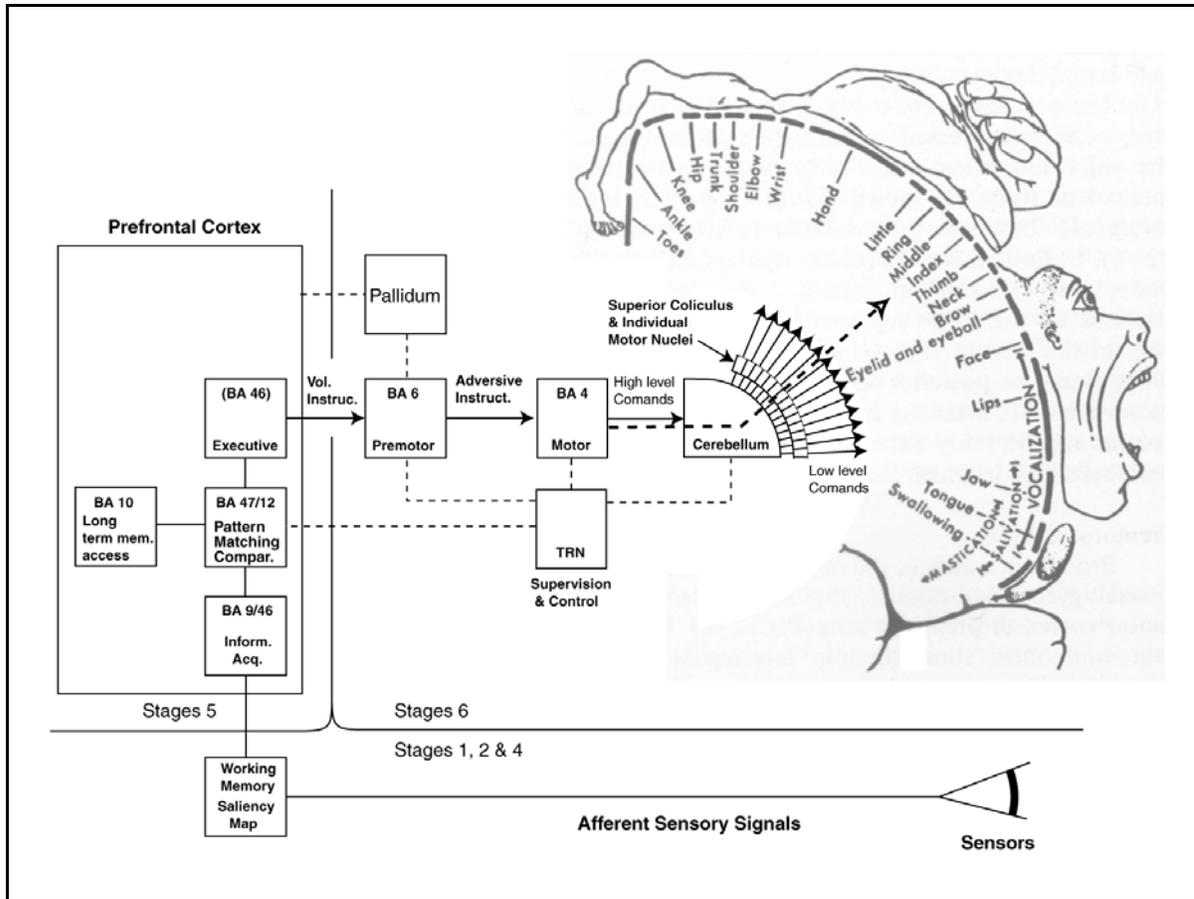


Figure 12.5.4-1 Block diagram and “action map” of the motor portion of the cerebral cortex. See text. Delineation of the stages of the neural system are shown for reference.

The area labeled vocalization on the right has been defined more precisely in the neural surgery literature, as have other areas of this depiction. An example appears in Rose⁷².

The figure begins on the left with a volition instruction issued by the executive, tentatively located in BA 46 of the prefrontal cortex. Such an instruction is very concise and may call for pointing the index finger in a specific direction. This instruction is passed to the premotor cortex (BA 6) where the instruction is interpreted in the light of the present posture of the subject and prepares a adversive instruction that is passed to the motor area of the cortex (BA 4). This adversive instruction includes commands to multiple muscles required to orient the finger as desired. However it does not include commands required to maintain the subjects balance while executing the desired instruction. The motor area is the first element of the motor system that issues a command signal that can be implemented by the musculatura. However, as noted, this command is typically not adequate.

In the absence of any other functional elements, such as the cerebellum, the command would be sent directly to the superior colliculus (and some individual neural nuclei) where it would be relayed to the appropriate muscles. The result is typically an ungainly effort to point the index finger as desired. Such a “default command” is shown by the dashed line in the figure leading to the index finger.

⁷²Rose, S. (1976) *The Conscious Brain*, Updated Ed. NY: Vintage Books pg 105

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The above brief discussion describes how the afferent motor system operates in the absence of any procedural learning. Such operation can be associated with the motions of a baby.

The role of the cerebellum is to coordinate a wide variety of sensory and muscular activities. It does this by accepting the coarse neural commands from the motor area and reinterpreting them in the context of the posture of the subject. The result is a broader range of commands intended to perform the desired action but without encountering unexpected consequences (such as falling over backwards) while turning the necessary parts of the body in order to point the finger as desired..

The broader range of commands required are coordinated by the cerebellum. This coordination includes both a relative amplitude component and a temporal component applied to each of the individual neuro-muscular signals. The result is a fully coordinated and smooth implementation of the original volition instruction (without any overshoot if performed within the ability of the efferent sensory system to monitor the activity. The action described is the result of procedural learning.

As noted in Section xxx, the cerebellum allocates only minimal area to the vision and auditory modalities. The visual modality relies primarily on its portion of the pulvinar and the auxiliary optical system to perform similar services to those of the cerebellum in order to minimize the time delay in the servo loops of the visual system. Similarly, the auditory modality uses its portion of the pulvinar to minimize the time delay associated with the alarm mode of CNS operation.

Since the efferent neural system operates totally in open loop mode, the overall system is designed to use the afferent sensory system to close a feedback loop. The sensory modalities observe the action and report back to the executive whether it was performed within the desired degree of precision. If not, the executive can alter its original volition instruction incrementally and wait for a report as to whether the action was performed more precisely. This operation of the entire feedback loop can be performed as many times as necessary. When performed to the executives satisfaction, the various instructions and commands can be recorded in appropriate memory elements.

XXX writing recently in xxx have provided data on the learning sequence used by babies to establish their motor memory baselines⁷³. They used a head mounted eye-tracker while the infant was becoming familiar with a carefully prepared play room. They note how six walking infants (14 months \pm 1 week) focus visual attention on the locations of its hands and feet during learning experiences. They did not address smooth pursuit activities. These would be foreign to such infants but worth studying at a later age. XXX studied the fixation of the eyes on the limbs up to the time the limb contacted the target. "These fixations indicate that infants often use online visual guidance to guide their limbs to the surface—that is, they watched their foot step over the obstacle—in contrast to adults and children who always break fixation of obstacles at least one step in advance."

While memory requirements to support volition instructions are relatively minor, the memory requirements placed on the cerebellum is immense. It is believed the major portion of the cerebellum is dedicated to procedural memory. The information stored in the saliency map (working memory) is highly compressed from the raw neural signals. However, over time, an immense amount of this information is stored in long term memory by a method and at locations not yet discovered.

Swanson has provided a recent but largely conceptual architecture for the human brain. In the context of this work, the terms of Swanson⁷⁴ can be translated using the following table.

⁷³XXX (2009) Head-mounted eye-tracking of infants' natural interactions: a new method E-T-R-A

⁷⁴Swanson, L. (2003) Brain Architecture. NY: Oxford Univ Press pg 135

Swanson label	Label used here	Brodmann area
Central pattern controllers	The executive	(BA 46)
Central pattern initiators	Premotor areas	BA 6
Central pattern generators	Motor areas	BA 4
Motor pattern learning	Cerebellum	
Motor neuron pools	Superior Colliculus	

The initial operation of the system in the absence of learning strongly supports the concept of an initial instruction and memory load (a bootstrap routine in computer language) derived during genesis. This initial load would ultimately derive from the genetic code.

The movements of subjects with significant injury to the cerebellum indicates the continued presence of the default signaling mode described above, along with increased participation in routine movements by the sensory modalities and the prefrontal cortex. Such additional activity is frequently reported as exhausting.

The pallidum is that portion of the basal ganglia most associated with motor functions. It appears to play a role in expanding the adversive instructions of the premotor areas similar to that the cerebellum plays in expanding the commands generated by the motor areas. However, the data is very sketchy. Alternate roles and implementations involving the pallidum cannot be ruled out.

Swanson extends his neuro-muscular concept to include the neuro-glandular domain as well (page 136). This subject is discussed in **Section xxx**. The operation of the neuro-glandular system parallels the above analysis. [xxx use swanson page 127]

12.6 Relational reasoning in the prefrontal lobe

Waltz et al. have provided good evidence as to reasoning within the prefrontal lobe⁷⁵. Their principle conclusion appears to be "that integration of relations is a specific source of cognitive complexity for which intact prefrontal cortex is essential." They assert, "There is a critical gap between the capacity to comprehend single relations and the capacity to integrate multiple relations." and cite several sources.

12.6.1 Pattern thinking and "Pattern Thinkers"

The operation of the brain as a pattern matcher and seeker of patterns in information has been a long-standing subject in psychology⁷⁶. Table 1 of this reference (**Figure 12.6.2-1**) provides a broad overview of the characteristics of pattern thinking in general. It is remarkably insightful.

⁷⁵Waltz, J. Knowlton, B. Holyoak, K. et al. (1999) A system for relational reasoning in human prefrontal cortex. Psychol Sci vol 10(2), pp 119-125

⁷⁶<http://ecomind.wikidot.com/process:patternthinking1>

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OVERALL CHARACTERISTICS	
• Pattern thinkers are <i>Generalists</i>	
• Pattern thinking contributes to a distinctive <i>Worldview & Paradigm</i>	
• Pattern thinking is <i>Transcontextual & Transdisciplinary</i>	
• Patterns are the material of <i>Neuronal Function</i> or are the substance of <i>Thinking</i>	
FOCUSES ON:	THINKING PROCESSES:
• <i>Patterns</i>	• <i>Recognizing</i> patterns – (cascading pattern extractions)
• <i>Relationships</i>	• <i>Analyzing functions & meanings</i>
• <i>Connections</i>	• <i>Analyzing</i> from <i>multiple perspectives</i>
• <i>Functions</i>	• <i>Situating</i> patterns in <i>contexts</i>
• <i>Meanings</i>	• <i>Locating</i> patterns in <i>contexts</i>
• <i>Adaptation</i>	• <i>Evaluating & Testing</i>
• <i>Complexity</i>	• <i>Modeling</i>
• <i>Recursiveness</i>	• <i>Organizing</i>
• <i>Models</i>	• <i>Categorizing</i>
• <i>Understandings</i>	• <i>Associating</i> – analogs, metaphors, etc.
• <i>Similarities & Differences</i>	• <i>Thinking Abductively</i>
CONCERNS	
• <i>“Difference”</i> is critical to pattern recognition and understanding	
• <i>Assumptions</i>	• <i>Systems</i>
• <i>Transformative Learning</i>	• <i>Complexity</i>
• <i>Context</i>	• <i>Connects & Disconnects</i>
NOTE: This table is compiled from: Bateson (1979/2002); Bloom (2004, 2006); Bloom & Volk (2007); Coward (1990); Hofstadter (1979); Lakoff & Johnson (1980); Thomas (1987); Volk & Bloom (2007); Volk, Bloom, & Richards (2007)	

Figure 12.6.2-1 Table of pattern thinking characteristics. The precise words in this table have been developed over a long period of introspection. Many of the terms are defined in greater detail on the cited website.

The subject has achieved new prominence due to the writings and speeches of Temple Grandin, a well known Autistic person and prolific author⁷⁷. Temple has gone one step farther and proposed that pattern thinking can take on three more specific forms within the same general context; picture thinking, pattern thinking and word thinking.

This author has long recognized himself as a pattern thinker in the Grandin context but with a strong reliance on graphic inputs. His photographic memory served him well through at least his mid fifties in acquiring vast amounts of information. His tendency has always been to place this information into a “framework,” which Temple and the community have preferred to label a “pattern.”

The graphic input capability is so strong, that I can write or sketch something and then throw the paper away. The image is permanently stored, in considerable detail, without further reference to the paper image. Reciting a paragraph under a specific figure in a chemistry text, without the text being present, once cost me an A in Chemistry 101 .

All of the writings of this author in neuroscience have been based on an attempt to

⁷⁷Grandin, T. (2013) The Autistic Brain. NY: Houghton Mifflin Harcourt

rationalize the literature and present it in a single consistent and conflict-free, framework. This has required the employment of a great deal of transdisciplinary material.

The use of the term pattern thinking in two different contexts is a problem within the psychology community. Several alternate terms might be used, artistic thinking in place of picture thinking and functional thinking in place of pattern thinking. Crossing disciplinary lines, artistic thinking and expression is the foundation of the copyright system in the USA while functional thinking is the foundation of the patent system in the USA.

Grandin has also attempted for the first time to define the previously nebulous concept of the autistic spectrum in clinical medicine; from the severely disabled at one extreme to the Einstein or Steve Jobs at the other extreme (page 16). She notes the high frequency of mini-Einsteins in Silicon Valley exhibiting one or more characteristics of autism based on the broader definition of the spectrum. This extension of the definition of the autism spectrum is one reason for the increased incidence of autism in recent years, *along with the very significant typographical error* in the 1994 edition of the "Diagnostic and Statistical Manual of Mental Disorders," (DSM) noted by Grandin (page 18). While widely discussed within the community, the error was not formally corrected until the DSM-5 of 2013.

12.7 Behavioral states and the prefrontal cortex

[xxx look at Swanson, chapter 6 of 2003 book]
[xxx look at Baars & Gage, page 295 of 2010 book, 2nd ed.]

12.8 Initial discussions of failure modes within the executive

As noted in the sections on prefrontal cortex (executive) failures, Bryson (page 34) has asserted that autistic "minds are distinguished by two unique features. First, an obstruction exists between the senses and the mind, or, put somewhat differently, the door to the outside (sensory) world is closed. Implied here is that incoming information may be incomplete or otherwise distorted." The implication is much less forceful than the assertion. "Second, information is stored in separate rather than conceptually or semantically related folders, thus resulting in precision at the expense of categorization and generalization." While Bryson's statements are based primarily on a conceptual framework, they clearly suggest a problem in the engine labeled "analytical information acceptance" in this figure, although the problem could equally well be associated with the "long term memory access" engine.

latest material from Chapter 15
2- Correlation
computational anatomy
blobs with reference

12.8.1 Failure modes following major cerebral surgical excisions

Petrides has provided a set of remarkable figures showing the results of major frontal and temporal lobe excisions involving humans and resulting in minimal (depending on the definition) performance impairment⁷⁸. The performance was evaluated on conditional tasks. He notes care was taken in all cases of frontal lobe excisions to avoid the speech area of Broca. **Figure 12.8.1-1** shows paired views of major excisions of the left frontal lobe based on the surgeon's drawings at the time of the operation. The pairs show the lateral and medial view of the left hemisphere except for the two sets at upper left which also include a view of the hemisphere from below. Similar sets of drawings applying to the right hemisphere and the temporal lobes are included in the Petrides paper. He asserts, "Excision of the frontal cortex, such as those illustrated do not cause any obvious motor or sensory defects and they

⁷⁸Petrides, M. (1991) Learning impairments following excisions of the primate frontal cortex *In* Levin, H. Eisenberg, H. & Benton, A. eds. Frontal Lobe Function and Dysfunction. NY: Oxford Univ Press Chap 13

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do not impair performance on conventional intelligence tests and various perceptual, linguistic, and memory tasks that have proven to be sensitive indicators of posterior cortical or mesial temporal lobe lesions.”

Such severe excisions strongly suggest one of two situations. Most likely, the left and right prefrontal cortices and most of the premotor areas are highly redundant. Alternately, a reflex arc exists at the highest level between the correlated sensory information available at the saliency map and the premotor areas of the frontal cortex, probably under the control of the TRN.

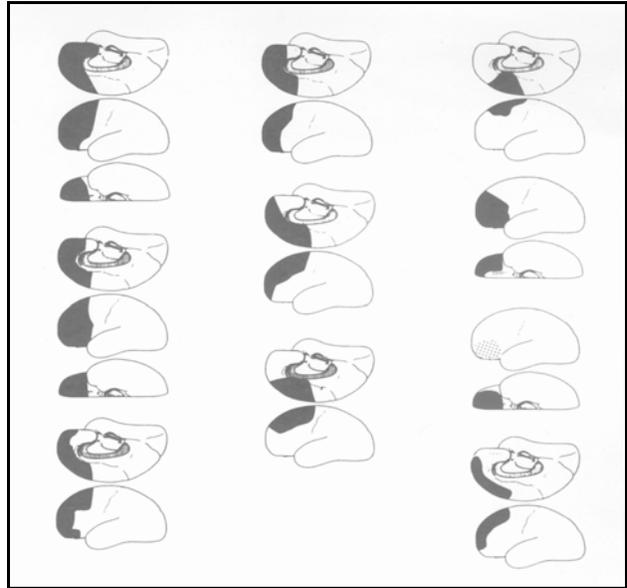


Figure 12.8.1-1 Drawing pairs of major cortical incisions of the left frontal lobe. See text. From Petrides, 1991.

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