E.A. Mayer and C.B. Saper (Eds.)
*Progress in Brain Research*, Vol 122

## CHAPTER 2

# Topography and relationships of mind and brain

Brent A. Vogt[1,]* and Orrin Devinsky[2]

[1] *Cingulum NeuroSciences Institute, 101 N. Chestnut St, Winston-Salem, NC 27101, USA and Wake Forest University School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157, USA*
[2] *New York University-Mount Sinai Comprehensive Epilepsy Center, 560 First Avenue-Rivergate 4th Floor, New York, NY 10016, USA*

## Introduction

Although the primary neuroscience literature does not directly address the mind, mentalistic perspectives are often used to frame broad issues of brain function. These concepts include attention, perception, stress, emotion, and pain. In order for neuroscience to participate in the Mind/Body debate, a physical definition of mind and its relationship to brain function is needed. The concept of mind considered by Descartes, Sherrington and others was an introspective view of self and emphasized the unitary and continuous nature of mental activity. Early efforts to distinguish the mind from the body, however, led to a dualism in which the physical/neurological origin and constraints on mind were not apparent. This view still dominates Western views of the mind even though the dependence of mental activity on internal and external events makes such a distinction counterproductive. As the Mind/Brain problem is clarified, the mechanics of Mind/Brain/Body interactions are open to discourse, investigation, and hypothesis testing. Some critical questions for neuroscience include the following: To what extent can the properties of mind be specified? Is there a neural basis for the theory of mind? To what extent is mental activity localized or distributed in the brain? How do various processing modes and links with executive systems relate to consciousness?

La Peyronie in 18th century France sought relations between mind and brain scientifically with postmortem tissue (Kaitaro, 1996). Although one may argue over his conclusions, he was among the first to presume that mind did not have a uniform distribution in the brain. The next two centuries of neurological observations and the recently acquired body of functional brain imaging under highly controlled neuropsychological conditions provide specific information about relationships between mind and brain that are pivotal to understanding Mind/Body interactions.

The mind is often defined as 'awareness of self', yet this concept itself can be misconstrued. If the mind is solely awareness of self, the mind might be expected to thrive outside the context of the body including neuronal activity in the brain. However, isolated, premature babies fail to gain weight and thrive (Schanberg and Field, 1987) and sensory stabilization experiments in isolation chambers lead to reduced intellectual performance, altered perceptions, hallucinations, and emotional changes (Bexton et al., 1954; Doane et al., 1959; Davis et al., 1960; Solomon et al., 1961). The notion that 'self' can exist independent of internal and external events is an extreme conclusion based on the philosophical Mind/Body duality and is not a part of neuroscience discourse.

---

*Corresponding author. Tel.: 336-716-8588; Fax: 336-716-8501; e-mail: bvogt@wfubmc.edu

At the other extreme, one might posit that all sensory and motor activity is mental activity and that the mind is equivalent to activity in most of the brain (e.g., Kandel, 1991). Spinal cord injury followed by appropriate rehabilitation, however, does not impair mental activity. Furthermore, Crick and Koch (1995, 1998) have argued that mammals are not aware of events in primary visual cortex and that explicit interpretation of visual scenes occurs in visual and polymodal association cortices. Logothetis and Schall (1989) provide elegant support for this notion with single unit recordings in monkey at different points along the visual cortical processing hierarchy. Although many neurons were driven by the retinal features of a stimulus, those in cortex of the superior temporal sulcus appeared to be driven by the perception of motion. Finally, synthesizing the visual image may depend on simultaneous and synchronous activity in primary visual and visual association areas because patients with blindsight following primary visual cortical lesions have non-conscious access to visual information but are unaware of what they can see (Devinsky, 1997).

Since mental activity may not extend to the spinal motor neuron and primary sensory cortices, the mind localization problem is a question of finding the essential networks that mediate mental activity in the forebrain. These networks comprise the focal point of Mind/Body research and therapy. The importance of neuroanatomical organization in assessing awareness and mental functions has been explicitly stated by Crick and Koch (1995) and supports the anatomical orientation of this review. Since it is unlikely that the entire brain is engaged equally in mental activity, the mind has a high probability of being located in parts of the cerebral cortex that underlie perception and mental activity.

Neuroscientific observations have not established the relationships between the mind and consciousness and there is no strategy for identifying the mind much less to localize it. One theoretical approach is to search for the neuronal correlates of consciousness as suggested by Crick and Koch (1995), however, such information is not available and it is unlikely that current methodologies for multiunit recording will succeed at this task. Frith (1992) suggests that understanding consciousness in terms of information processing requires a cognitive mechanism that is constantly associated with consciousness, whether or not the processing mechanism itself is available for observation. This may require coordinated activity in a number of distributed processing modules and/or persistent processing in one or two profoundly important regions. Several models relating specialized processing modules, phenomenal consciousness, executive and other functional and cognitive subsystems have been proposed (Block, 1995). One of the problems of neuroscience is to identify the morphological substrates in these and similar models and to assess interactions among their processing subsystems. They are, however, beyond the scope of this assessment.

The present analysis considers the localization of mental activity in cortical regions of confluence among cytoarchitectural areas. It suggests that the binding problem may be solved by understanding the interconnections of these regions. Finally, the location of mind per se and mechanisms of consciousness are not addressed here. Instead, the high probability of association between mental activity and the mind is used here to suggest where the mind is located in the brain.

## Mental activity and the cortical confluence regions

In order to avoid the pitfalls inherent in a strict Mind/Body dualism, the definition of mind can be extended to the following:

> Mind is mental activity associated with internal and external awareness, intentions, and memories of self.

Each of these components are critical to mental activity and this perspective does not make mind dependent on a sensory modality or motor output. Indeed, the intention to move is an essential activity of mind, not a particular movement itself. Similarly, long-term memories establish the motivational context of intentions or willed actions. Although little is known about the very long-term storage of self-oriented information in the brain, lesion studies indicate that some regions are more important to internal and external awareness of self than are others, while functional imaging lends insight into localizing the intentions, imagery, and logical activities of mind.

As stated earlier, it is unlikely that the entire cerebral cortex participates equally in mental function. Additionally, it has been known for some time that serial processing of cortical information from single sensory modalities to 'higher order' integration sites does not occur in a fashion that can account for unified perceptions and a coherent awareness of self. Efforts to solve the binding problem emphasize the failure of serial processing models. We propose that there are two sites in the cortex that fulfill the definition of mind provided above. These are the cingulofrontal and parietotemporal confluence regions.

> The cingulofrontal and parietotemporal confluence regions bind the internal and external features of self and employ the various motor and cognitive systems to implement intentions.

These sites are probably not involved in binding features into entities as discussed by Damasio (1989) nor do they address the broader issues of binding throughout the cerebral cortex (Sejnowski, 1986). The neural codes from early convergences and memories of self are used by the cingulofrontal and parietotemporal convergence regions to implement the intentions of self.

## Localizing mental activity with lesions

Anterior cingulate cortex is essential for mental activity. Bilateral lesions of the anterior cingulate gyri produce akinesia, mutism, indifference to noxious stimuli and surroundings, incontinence, and lack of spontaneity (Nielsen and Jacobs, 1951; Barris and Schuman, 1953). Akinetic mute patients appear conscious, their eyes are open, deep tendon reflexes and muscle tone may be normal, but these patients show minimal or no spontaneous motor or verbal behavior. They lack intention and willed actions. Other evidence supports the hypothesis that anterior cingulate cortex is essential for mental activity and initiation and regulation of behavior. Cannon and his colleagues emphasized the critical role of anterior cingulate cortex in regulating aggressive behaviors that are initiated in the midbrain (Bard and Mountcastle, 1948). Medial cortical lesions remove sensory guidance and control of reflexes and suggest a cortical localization of mind. Glucose metabolism is reduced in perigenual cingulate cortex in depressed individuals and may indicate that this region is involved in the disease and, hence, the initiation of behavior (Drevets et al., 1997; Mayberg, 1997). Finally, seizure activity in midcingulate cortex (area 24′) is associated with obsessive-compulsive disorder and this behavior resolves following surgical removal of this region (Levin and Duchoway, 1991).

The crucial role of anterior cingulate cortex to willed actions and mental activity is provided by observations of individuals with unilateral lesions in this region following occlusion of the proximal part of the anterior cerebral artery. Such lesions resulted initially in mutism and paucity of movement or akinesia, although these patients were alert and oriented to time and place (Chan and Ross, 1997). Two to four weeks after the vascular event there was a continued reduction in spontaneous speech which was monotonic as well as reduced contralateral movements that did not appear to have been consciously driven by the patient such as those of the hand. In fact, one patient with a large right anterior cingulate/supplementary motor cortex infarct reported that his left hand was alien because it operated 'against his will'. One interpretation of these findings is that his willed actions were generated in his left anterior cingulate cortex. Review of a broad neurological and neurobiological literature (Devinsky et al., 1995) suggests that anterior cingulate cortex is pivotal to internal and external awareness of self and intentions.

Many of the neurological impairments suffered by Phineas P. Gage may have been due to damage in the anterior cingulate and adjacent orbitofrontal and dorsomedial prefrontal cortices. Although his sensorimotor faculties were intact and his linguistic and cognitive functions fairly well preserved, he could not select among appropriate responses, had an altered personality, and was socially inappropriate. He was described as fitful, irreverent, indulging at times in the grossest of profanity, impatient, vacillating, a child in his intellectual capacity and manifestations. Recent analysis of the skull and tamping iron that produced the cortical damage in Gage's brain has been made by Damasio et al. (1994). This reconstruction of the placement of the tamping iron in the brain suggests that the primary lesion site in Gage's brain was in perigenual cingulate cortex and adjacent orbitofrontal and mediodorsal prefrontal areas. Since sociopathic behaviors and altered personality have also been reported in patients with medial and orbitofrontal cortex damage (Damasio et al., 1990), this region appears to be necessary for mental activity.

Contralateral neglect, impaired volition and movement, and reductions in spontaneous speech are not unique consequences of lesions in anterior cingulate cortex. Although an account of lesion size and placement must be made, lesions in posterior parietal and prefrontal cortices can produce these effects. Neglect following frontal and parietal lesions may be specialized such that ophthalmokinetic neglect is more frequent following parietal lobe lesions, while melokinetic neglect more often follows frontal lesions (Bisiach et al., 1995), and both regions have also been implicated in intention (Stuss and Benson, 1984; Andersen, 1995). Prefrontal lesions can produce motor neglect and interfere with specific executive functions (Rizzolatti et al., 1983) and, to the extent that they disrupt an internal sense of self and produce apathy and denial of illness (anosognosia), are likely critical for mental functions. Although large lesions of prefrontal cortex severely impair mental activity, it is possible that the mind is much less impaired by loss of small parts of lateral prefrontal cortex. The extent to which subregions in frontal and parietal cortices contribute to mental function and how this relates to activity in anterior cingulate cortex can be addressed to some extent with functional imaging techniques as discussed below. Failure to produce deficits associated with intentions and self awareness following lesions in the parietotemporal region may be due to lack of equivalent and bilateral destruction in most cases, whereas bilateral destruction of homologous regions in anterior cingulate cortex is more likely due to the pattern of blood flow impairment and hemorrhage produced by anterior cerebral and communicating artery lesions.

Before moving to functional imaging assessments, let us contrast the neurological deficits following damage in regions that are essential to mental activity with those that are **not** essential to the internal and external awareness of self. One dramatic instance of an ineffective ablation is that in retrosplenial cortex and possibly the fornix after removal of an arteriovascular malformation (Valenstein et al., 1987). Following surgical recovery, this individual could not return to work because of persistent anterograde memory impairment. Although he was oriented to time and place and had relatively intact remote memory, recall of events over the past four years was difficult. Remarkably, his general intellectual functions, language, and praxis were intact. There are no reports of impaired executive or other 'frontal lobe' functions including personality, behavioral initiation or suppression problems. It seems, therefore, that cortical and subcortical regions involved in short-term memory formation may limit the range of new behaviors but they are not essential for mental activity and personality per se. Some structures involved in short-term memory that may be viewed as non-essential to mental activity include the anterior thalamic nuclei, mammillary bodies, retrosplenial cortex, parahippocampal cortex, and the hippocampus. Similarly, lesions in primary and association sensory and motor cortices impair restricted aspects of perceptual or motor behavior, but not of mind or personality.

## Localizing mental activity with functional imaging

Although brain lesion outcomes implicate many parts of the cerebral cortex in mental activity, localization is difficult in highly interconnected and distributed processing systems. Damage to a single component of a distributed network may reflect composite deficits associated with direct damage as well as disruption of one or more deafferented areas. In many instances cortical lesions may not be equal in extent and bilateral providing for recovery of function. Although bilateral lesions of anterior cingulate cortex are available, for example, it is heavily interconnected with prefrontal area 46 and these two regions are frequently but not always coactivated in functional imaging studies. In contrast to brain lesion studies, functional imaging provides localization information for repetitive tasks and methods for assessing subfunctions of components in a distributed network. Information gleaned with this strategy, however, is influenced by signal smoothing, subtraction protocols, system habituation, signal averaging, and statistical criteria. Each of these analytical issues raises difficulties in defining the limits of an active region. This strategy also requires that activated sites be uniform in each case in a standardized stereotaxic space; a requirement that is often not met in the highly variable human brain. In spite of these shortcomings, many testing paradigms support the contention that anterior cingulate and adjacent medial prefrontal cortices as well as parietotemporal cortex are pivotal to mental activity.

Activation of anterior cingulate and dorsolateral prefrontal cortices during a visually guided, divided attention task led Corbetta et al. (1991) to suggest that these two regions are involved in response selection in cognitively challenging situations. The proposition of these authors that anterior cingulate cortex was engaged in response selection was a pivotal step toward understanding the contribution of this region to brain function. Support for this hypothesis was provided later in a verbal response selection task (Raichle et al., 1994) as well as during the standard Stroop (Pardo et al., 1990; Derbyshire et al., 1998) and counting Stroop (Bush et al., 1998) tasks. In addition to activation of midcingulate cortex in the various Stroop paradigms, other cortical areas are activated including prefrontal areas 46, 44/45, 9 and 10, the inferior parietal and retrosplenial areas, and the anterior insula. The persistent involvement of midcingulate cortex and its extension to dorsal perigenual area 32 in functional imaging studies emphasizes the necessary contribution of this region to response selection.

Another perspective on response selection is embodied in the studies of willed actions (Frith et al., 1991). When responses in a response selection task were open-ended and involved a deliberate choice, blood flow increased in anterior cingulate areas 24 and 32 as well as prefrontal area 46 and posterior temporal cortex. Response selection/willed action tasks require assessment of the motivational significance of a particular outcome and working memory during the selection process. Such a dual function likely requires involvement of anterior cingulate cortex in response selection for motivationally relevant cognitive and behavioral outcomes. The massive and reciprocal connections between these anterior cingulate and prefrontal cortices are well known (Vogt et al., 1979; Baleydiere and Mauguiére, 1980; Goldman-Rakic et al., 1984; Vogt and Pandya, 1987; Barbas and Pandya, 1989). Such connections suggest that these areas often operate in parallel, since the response selection function requires an intact working memory and contributions from prefrontal cortex (Goldman-Rakic, 1987; Fuster, 1995).

During motor imagery, Decety et al. (1994) observed activation of anterior cingulate areas 24 and 32, lateral prefrontal areas 6, 9, 8, and 46 and inferior parietal area 40. These authors noted that supplementary motor cortex was not active during motor imagery suggesting a functional dissociation of medial and lateral premotor areas. In this context, it is interesting that Bancaud and Talairach (1992) stimulated midcingulate cortex and produced the desire to leave the room; cognitive activity that precedes the actual formation of a movement strategy and belies the motivational functions of midcingulate cortex. Thus, an important part of establishing motivationally relevant responses is associated with imagery, motivational significance of motor outcomes, and goal orientation (Vogt et al., 1997).

Another strategy for localizing mental activity is a consideration of those structures involved in the logic of mental activity. Goel et al. (1997) engaged subjects in deductive and inductive reasoning problems involving three sentences that did or did not, respectively, support a particular conclusion during scanning sessions. They found that subtraction of blood flow during deductive reasoning from that during inductive reasoning showed elevated blood flow in medial prefrontal cortex including areas 8, 9, 24, and 32. In addition to localizing the site crucial for inductive reasoning, they did not coactivate prefrontal area 46 or lateral parietotemporal areas. This is one of the few instances in which anterior cingulate and prefrontal cortical activity has been dissociated and suggests the essential role of the former region in mental activity. The close association between mental processing and inductive reasoning may be due to the persistent use of inconclusive information to interpret the significance of sensory information and predict outcomes.

One facet of mental activity is the ability to interpret the mental state of others. Mentalizing story comprehension tasks activate medial cortex between areas 8 and 9 (Mazoyer et al., 1993). 'Theory of mind' stories that require attribution of mental states to characters also activate medial area 8 and midcingulate cortex (Fletcher et al., 1995). The latter activation was demonstrated by subtracting blood flow produced during 'physical' stories that did not require mental state attribution or stories with unconnected sentences from blood flow evoked by the 'theory of mind' stories. Although posterior cingulate cortex was additionally activated in the latter study, this does not mean that areas 23 and 31 are involved in mental activity but, rather, that the stories themselves require a personal orientation in space that is organized in posterior cingulate cortex. Hence, area 23 has neuronal discharges coded for large visual fields (i.e., picture content stimuli and grating rather than simple shapes and other features; Olson et al., 1993). Hirono et al. (1998) have shown a relationship between glucose hypometabolism in posterior cingulate cortex in Alzheimer's disease and spatial disorientation. Therefore, coactivation of posterior cingulate cortex in mental imagery and mentalizing tasks likely represents a visuospatial orientation rather than a function of mind per se and, if the posterior cingulate cortex were missing, it is likely that subjects could still perform 'theory of mind' tasks.

## The cingulofrontal and parietotemporal confluence regions: primary processors of the mind

Lesion and functional imaging studies together show that the primary sites of mental activity are the confluence regions between cingulate and medial prefrontal cortices and that between lateral parietal and temporal cortices. These two confluence regions are outlined in Fig. 1 as are the relevant cytoarchitectural areas. Although many other areas may contribute to activity in these regions including lateral prefrontal and posterior cingulate cortices in the normally active brain, lesion and imaging studies do not support a pivotal contribution to mental activity of these areas. The confluence regions, however, may not be sufficient for mental activity or normal functioning of the mind because complete uncoupling of them from internal and external stimuli as well as skeletomotor and visceral outputs would render these regions and the mind dysfunctional.

Functional imaging studies emphasize unique or coactivation of a number of areas in the rostral and medial cerebral cortex. These include areas 8, 9, 32, 24, and 24′. This region may participate in the activity of many networks to the extent that even 'purely sensory' processing may require significance coding and an assessment of motivational relevance. It is highly interconnected with lateral prefrontal area 46 that provides information for working memory and the temporal binding of behavioral sequences and plans (Fuster, 1995). Thus, the cingulofrontal confluence region provides the data upon which response selection among motivationally relevant cognitive and behavioral outputs is made. Activity in other cortical areas may not be required for reasoning, willed actions, and the motivational relevance of information processing. Certainly the amygdala has significance codes for simple sensory stimuli that require stereotypical reflexes. However, when these responses need modification or complex interpretations and selection among responses, cortical inputs are employed. Since the cingulofrontal and parietotemporal confluence regions appear to be critical for decision making in relation to the internal/external and motivational parameters of self, they are essential links in networks engaged by mental activity for processing self-significant information. Therefore, fundamental components of mind are located in the cingulofrontal and parietotemporal confluence regions.

## Lateralization of mental activity

The right hemisphere may dominate awareness and image of self and the relation of self, visuospatially

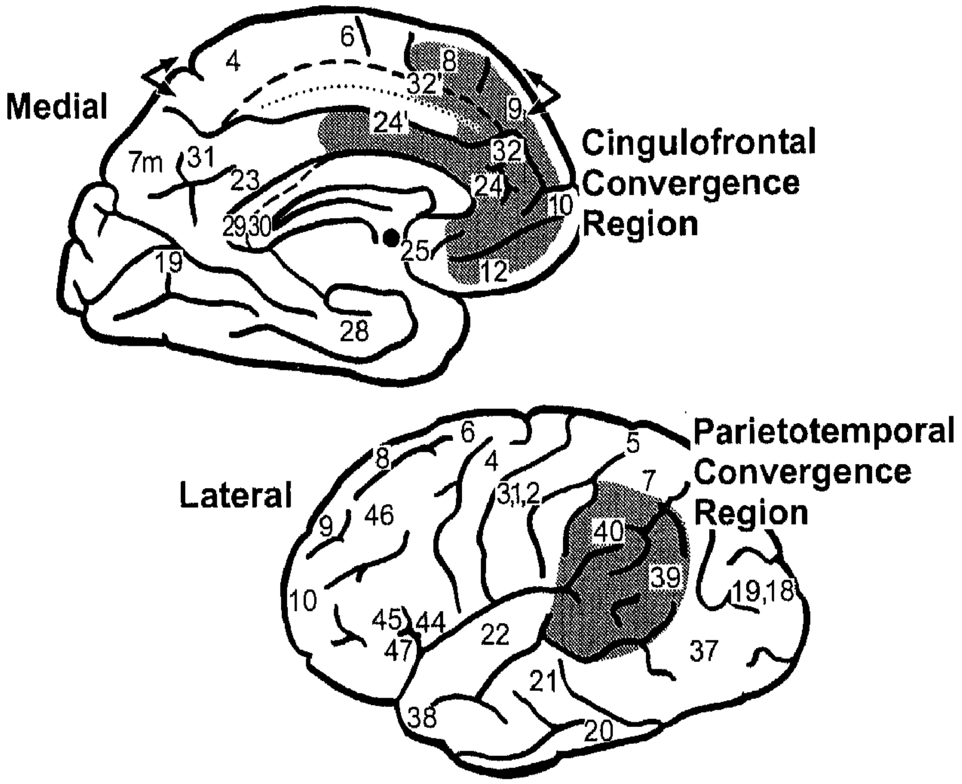

Fig. 1. The medial and lateral surfaces of the human brain are shown with Brodmann's areas. The two arrow pairs on the medial surface indicate cortex that was warped dorsally to account for opening part of the cingulate sulcus; the fundus of which is marked with a dotted line. The dashed line at the splenium of the corpus callosum represents the fundus of the callosal sulcus and shows that the retrosplenial areas 29 and 30 are in the depths of this sulcus. The two shaded regions are an approximate outline of the regions that we propose dominate mental activity and, as such, represent the primary processors of the mind as discussed in the text. The cingulate motor areas in the depths of the cingulate sulcus and visceromotor control cortex in area 25 are not viewed as part of the cingulofrontal confluence area that is necessary for mental function.

and psychically, to the environment (Devinsky, 1997). Acute lesions of the right hemisphere more severely disrupt the sense of self than left-sided lesions. Right hemisphere lesions can result in failure to recognize profound deficits as noted above, such as cortical blindness or left-sided hemiplegia (anosognosia), respond appropriately to recognized deficits (anosodiaphoria), or attend to the left half of extrapersonal and personal space. They can also cause the delusional belief that duplicate persons are impersonating well-known persons or delusional reduplications (Ruff and Volpe, 1981; Malloy et al., 1992; Signer, 1992). The right hemisphere may dominate our sense of self and lesions in the right parietal lobe can impair our body image. Left-sided neglect, anosognosia, and anosodiaphoria can be explained by destruction of a module of cortex controlling body image and physical relations of self to the environment.

Although the left hemisphere has been most often implicated in language, the right hemisphere has a role in prosody or interpreting the meaning of words by the way in which they are stated (Bryden and Ley, 1983). Goldberg and Podell (1995) discuss some of the observations that lead to the suggestion that the right hemisphere is critical for exploratory processing of novel cognitive situations for which there are no pre-existing codes or strategies, whereas the left hemisphere is critical for processing based on pre-existing representations and routine cognitive strategies. As they point out, the novelty-routinization hypothesis emphasizes the importance of instructional biases that accompany a task. An ambiguous task is likely to depend on the right hemisphere.

The novelty-routinization hypothesis can be assessed with functional imaging studies that engage some part of the cingulofrontal confluence region. Cognitively challenging tasks can activate the right cingulofrontal confluence region (Corbetta et al., 1991; Bench et al., 1993; Raichle et al., 1994; Bush et al., 1998). Although the left region is required for inductive reasoning (Goel et al., 1997) and performance on the sad Stroop task (George et al., 1994), interpreting 'theory of mind' stories appears to involve both hemispheres to some extent (Fletcher et al., 1995). Reasoning, processing of cognitively challenging information, assessment of emotionally charged faces, and 'mentalizing' functions may require both hemispheres even though studies of cortical damage lead to intriguing hypotheses about lateralization of functions. The specific contributions of each hemisphere to mental activity are not fully understood.

## Distributed mental activity and the unified mind

To the extent that there are two cortical sites in both hemispheres engaged in mental activity, perception of a single mind requires an explanation. Bogen (1986) considered issues relating to the duality of mind in the intact brain from the perspective of lateralization of function. The duality of mind associated with lateralization to either of the confluence regions alone is partially solved by contralateral callosal connections for each region. Either hemisphere can contribute to recovery of function following unilateral lesions and different contributions may be made by each hemisphere but joined by callosal connections. Thus, lateralization of functions do not interfere with a unified perception of self in either confluence region. Furthermore, if the cingulofrontal confluence region were the only primary site necessary for mental activity, activity in this region would represent the perceptual whole. However, the presence of two confluence regions requires solving what is often termed the 'binding problem'. How do we experience existence through a unified sense of self that seamlessly joins external and internal stimuli, memory, plans, emotions, and reflective thought in spite of distributed parallel processing in the cerebral cortex?

One attempt to solve the binding problem evolved naturally from the study of corticocortical connections. Serial connections from primary sensory to sensory association and then to multimodal areas is a sequence that would solve the problem by having a terminal site in the cortex that receives unique and highly processed inputs and is also interconnected with motor systems to control skeletomotor and autonomic activity. Numerous studies of monkey cortex failed to identify such an area. Furthermore, functional imaging studies support the concept of two or more cortical areas operating in parallel rather than converging on a single 'higher order' association area.

In terms of the two confluence regions, crucial corticocortical connections could subserve mental unity only if it can be shown that the cingulofrontal and parietotemporal confluence regions are interconnected. Connections of the human cerebral cortex are not known, however, and the connections of key parts of the confluence regions in human cortex do not appear to have counterparts in the monkey. Much of midcingulate cortex and areas 39 and 40 are difficult to homologize among primate species and this will continue to hamper efforts to understand mechanisms that subserve the unity of mind.

Another mechanism for binding activity in the two confluence regions is with a common input from a subcortical structure such as the intralaminar and midline thalamic nuclei. The system for processing noxious stimuli provides a means of assessing the potential role of these thalamic nuclei in consciousness and binding. As discussed in more detail in Chapter 16 of this volume, the midline and intralaminar thalamic nuclei have profound connections with anterior cingulate cortex. Although we do not know if cortex in the parietotemporal confluence region in human receives similar projections, we do know that noxious stimuli activate area 40 as well as other somatosensory areas (Svensson et al., 1997). These nuclei contain nociceptive neurons and blocking activity in this part of thalamus blocks nociceptive activity in anterior cingulate cortex (Sikes and Vogt, 1992). Since the cingulofrontal and parietotemporal confluence regions are primary components of the mind, noxious stimuli can directly drive neurons in both regions and engage affective, body orientation, and response selection patterns. In the instance of pain processing, the noxious stimulus directly drives the relevant response circuits via the intralaminar and midline thalamic nuclei. Thus, sensory or cognitive driving in combination with common circuitry in a parallel processing system may provide for unified perceptual events.

The common input mechanism provides for temporal linking of activity in divergent cortical regions and is similar to the proposition that massive and parallel networks are functionally synchronized to produce 40 Hz discharges by projections from the midline and intralaminar thalamus (Llinas and Ribary, 1993). Although this assures a common temporal pattern of discharge, it is not clear how this synchronization itself via a common input leads to binding of mental activity into a unified mind. Although it is unlikely that these thalamic nuclei operate like a 'searchlight', this mechanism might help to explain binding at the level of confluence regions, if the regions were themselves interconnected.

The binding problem for uniform mental activity may be solved in a number of ways. First, there may be just a few primary confluence regions that provide for the essence of mental activity such as willed actions, intentions, imagery, intuitive logic, and integration of the internal and external features of self. Second, sensory driving via the midline and intralaminar thalamic nuclei could provide for synchronizing activity in the confluence regions themselves and/or in other relevant networks. Third, homotopic callosal and ipsilateral connections between the cingulofrontal and parietotemporal regions would result in the final stage of binding parallel activities in distributed structures into a single mental event.

## Therapeutic implications of localizing the mind to two confluence regions

From a neuroscientific perspective, an understanding of functional activity in the cingulofrontal and parietotemporal confluence regions is essential for studies that seek to identify biological mechanisms whereby mental activity regulates the body and, hence, Mind/Body interactions. This emphasis on a few critical regions does not preclude involvement in many other telencephalic structures that are engaged in particular sensorimotor events and in the activities of parallel and distributed networks such as those in lateral prefrontal cortex and sequential and distributed processing in sensory systems. These localizations simply emphasize that there are regions essential to most mental activity, that are likely the location of the mind, and that cannot be overlooked in terms of dominant network functions during mental activity. The profound importance of the anterior cingulate cortex itself has been observed by others, including Damasio (1994), who observes that it is a 'fountainhead' that constitutes the source of energy for both external and internal actions.

The cingulofrontal confluence region provides a target for drug, rehabilitation, and meditation strategies for modifying Mind/Body interactions. Two examples of such possibilities can be provided in terms of psychological modifications of Mind/Brain/Body relationships. The first example is provided in studies of cerebral blood flow during hypnosis. In a study by Rainville et al. (1997), hypnosis was used to modify the unpleasantness of noxious stimuli. High levels of unpleasantness were associated with elevated blood flow in midcingulate cortex, while blood flow in the anterior insula was not selectively altered by unpleasantness of the stimuli. Although affect is not localized in midcingulate cortex (Vogt et al., 1997), hypnotic regulation of midcingulate cortex may be related to its involvement in mental imagery and response selection in relation to motivationally relevant stimuli. A second example of the potential of activations of the cingulofrontal confluence region to provide therapeutic relief is that suggested for motor imagery. Decety (1995) suggested that motor imagery itself may provide a strategy for stimulating recovery of motor function following damage to the central nervous system. From the perspective of Mind/Body interactions, such responses and their close relationship to mental activity suggest that the cingulofrontal confluence region should be a morphological target of future efforts to improve Mind/Body interactions and to counteract pathological processes that influence mental functions.

Therapies based on mentalistic strategies can be guided by testable hypotheses and neuroscience is on the verge of assessing the mechanisms of action of complex approaches to neurological and psychiatric diseases like those embodied by traditional/holistic medicine. A crucial link to future efforts will be hypothesis-driven experiments using functional imaging modalities. The neurobiology of Mind/Brain/Body interactions will inevitably focus on those regions in the brain that are primarily associated with mental activity including the cingulofrontal and parietotemporal confluence regions.

## References

Andersen, RA. (1995) Encoding of intention and spatial location in the posterior parietal cortex. *Cereb. Cort.*, 5: 457–469.

Baleydier, C. and Mauguière, F. (1980) The duality of the cingulate gyrus in monkey. Neuroanatomical study and functional hypotheses. *Brain*, 103: 525–554.

Bancaud, J. and Talairach, J. (1992) Clinical semiology of frontal lobe seizures. *Adv. Neurol.*, 57: 3–58.

Barbas, H. and Pandya, D.N. (1989) Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. *J. Comp. Neurol.*, 286: 353–375.

Bard, P. and Mountcastle, V.B. (1948) Some forebrain mechanisms involved in expression of rage with special reference to suppression of angry behavior. *Res. Nerv. Ment. Dis.*, 27: 362–404.

Barris, R.W. and Schuman, H.R. (1953) Bilateral anterior cingulate gyrus lesions. *Neurology*, 3: 44–52.

Bexton, W.H., Heron, W. and Scott, T.H. (1954) Effects of decreased variation in the sensory environment. *Can. J. Psychol.*, 8: 70–76.

Bench, C.J., Frith, C.D., Grasby, M., Friston, K.J., Paulesu, E., Frackowiack, R.S.J. and Dolan, R.J. (1993) Investigations of the functional anatomy of attention using the Stroop test. *Neuropsychologia*, 31: 907–922.

Bisiach, E., Tegner, R., Ladavas, E., Rusconi, M.L., Mijovic, D. and Hjaltason, H. (1995) Dissociation of ophthalmokinetic and melokinetic attention in unilateral neglect. *Cereb. Cort.*, 5: 439–447.

Block, N. (1995) On a confusion about the function of consciousness. *Behav. Brain Sci.*, 18: 227–287.

Bogen, J.E. (1986) Mental duality in the intact brain. *Bull. Clin. Neurosci.*, 51: 3–29.

Bryden, M.P. and Ley, R.G. (1983) Right-hemispheric involvement in the perception and expression of emotion in normal humans. In: K.M. Heilman and P. Satz (Eds.), *Neuropsychology of Human Emotion*, Guilford Press, New York, pp. 6–45.

Bush, G., Whalen, P.J., Rosen, B.R., Jenike, M.A., McLnerney, S.C. and Rauch, S.L. (1998) The counting Stroop: an interference task specialized for functional neuroimaging-validation study with functional MRI. *Hum. Brain Mapp.*, 6: 270–282.

Chan, J.-L. and Ross, E.D. (1997) Alien hand syndrome: influence of neglect on the clinical presentation of frontal and callosal variants. *Cortex*, 33: 287–299.

Corbetta, M., Miezin, F.M., Dobmeyer, S., Shulman, G.L. and Peterson, S.E. (1991) Selective and divided attention during visual discriminations of shape, colorm and speed: functional anatomy by positron emission tomography. *J. Neurosci.*, 11: 2383–2402.

Crick, F. and Koch, C. (1995) Are we aware of neural activity in primary visual cortex? *Nature*, 375: 121–123.

Crick, F. and Koch, C. (1998) Consciousness and neuroscience. *Cereb. Cort.*, 8: 97–107.

Damasio, A.R. (1989) The brain binds entities and events by multiregional activation from convergence zones. *Neural Comp.*, 1: 123–132.

Damasio, A.R. (1994) *Descartes' Error.* G.P. Putnam's Sons, New York.

Damasio, A.R., Tranel, D. and Damasio, H. (1990) Individuals with sociopathic behavior caused by frontal damage fail to respond autonomically to social stimuli. *Behav. Brain Res.*, 41: 81–94.

Damasio, H., Grabowski, T., Frank, R., Galaburda, A.M. and Damasio, A.R. (1994) The return of Phineas Gage: clues about the brain from the skull of a famous patient. *Science*, 264: 1102–1105.

Davis, J.M., McCourt, W.F. and Solomon, P. (1960) Effect of visual stimulation on hallucinations and other mental experience during sensory deprivation. *Am. J. Psychiatry*, 116: 889–908.

Decety, J., Perani, D., Jeannerod, M., Bettinardi, V., Tadary, B., Woods, R., Mazziotta, J.C. and Fazio, F. (1994) Mapping motor representation with positron emission tomography. *Nature*, 371: 600–602.

Decety, J. (1995) Can motor imagery be used as a form of therapy? *J. NIH Res.*, 7: 47–48.

Derbyshire, S.W.G., Vogt, B.A. and Jones, A.K.P. (1998) Pain and Stroop interference tasks activate separate processing modules in anterior cingulate cortex. *Exp. Brain Res.*, 118: 52–60.

Devinsky, O. (1997) Neurological aspects of the conscious and unconscious mind. *Ann. NY Acad. Sci.*, 835: 321–329.

Devinsky, O., Morrell, M.J. and Vogt, B.A. (1995) Contributions of anterior cingulate cortex to behavior. *Brain*, 118: 279–306.

Doane, B.K., Mahatoo, W., Heron, E. and Scott, T.H. (1959) Changes in perceptual function after isolation. *Can. J. Psychol.*, 13: 210–215.

Drevets, W.C., Price, J.L., Simpson, J.R., Todd, R.D., Reich, T., Vannier, M. and Raichle, M.E. (1997) Subgenual prefrontal cortex abnormalities in mood disorders. *Nature*, 386: 824–827.

Fletcher, P., Happé, F., Frith, U., Baker, S.C., Dolan, R.J., Frakowiack, R.S.J. and Frith, C.D. (1995) Other minds in the brain: a functional imaging study of 'theory of mind' in story comprehension. *Cognition*, 57: 109–128.

Frith, C.D. (1992) Consciousness, information processing and the brain. *J. Psychopharmacol.*, 6: 436–449.

Frith, C.D., Friston, K., Liddle, P.F. and Frackowiack, R.S.J. (1991) Willed actions and the prefrontal cortex in man: a study with PET. *Proc. R. Soc. Lond. B.*, 244: 241–246.

Fuster, J.M. (1995) Memory and planning: Two temporal perspectives of frontal lobe function. In: H.H. Jasper, S.P.S. Riggio and Goldman-Rakic (Eds.), *Epilepsy and the Functional Anatomy of the Frontal Lobe, Advances in Neurology*, Vol 66, Raven Press, New York, pp. 9–20.

George, M.S., Ketter, T.A., Parekh, P.I., Rosinsky, N., Ring, H., Casey, B.J., Trimble, M.R., Horwitz, B., Herscovitch, P. and Post, R.M. (1994) Regional brain activity when selecting a response despite interference: An $H_2^{15}O$ PET study of the Stroop and an emotional Stroop. *Hum. Brain Mapp.*, 1: 194–209.

Goel, V., Gold, B., Kapur, S. and Houle, S. (1997) The seats of reason? An imaging study of deductive and inductive reasoning. *Cog. Neurosci. Neuropsychol.*, 8: 1305–1309.

Goldberg, E. and Podell, K. (1995) Lateralization in the frontal lobes. In: H.H. Jasper, S. Riggio and P.S. Goldman-Rakic (Eds.), *Epilepsy and the Functional Anatomy of the Frontal Lobe, Advances in Neurology*, Vol 66, Raven Press, New York, pp. 85–96.

Goldman-Rakic, P.S. (1987) Circuitry of the prefrontal cortex and the regulation of behavior by representational memory. In: V.B. Mountcastle, F. Plum and S.R. Geiger (Eds.), *Handbook of Physiology, Part 1 The Nervous System*, Chapter 9, American Physiological Society, Bethesda, MD, pp. 373–417.

Goldman-Rakic, P.S., Selemon, L.D. and Schwartz, M.L. (1984) Dual pathways connecting the dorsolateral prefrontal cortex with the hippocampal formation and parahippocampal cortex in the rhesus monkey. *Neuroscience*, 12: 719–743.

Hirono, N., Mori, E., Ishii, K., Ikejiri, Y., Imamura, T., Shimomura, T., Hashimoto, M., Yamashita, H. and Sasaki, M. (1998) Hypofunction in the posterior cingulate gyrus correlates with disorientation for time and place in Alzheimer's disease. *J. Neurol. Neurosurg. Psychiatry*, 64: 552–554.

Kaitaro, T. (1996) La Peyronie and the experimental search for the seat of the soul: neuropsychological methodology in the eighteenth century. *Cortex*, 32: 557–564.

Kandel, E.R. (1991) Brain and behavior. In: E.R. Kandel, J.H. Schwartz and T.M. Jessell (Eds.), *Principles of Neural Science*, Elsvier, New York.

Levin, B., Duchowny, M. (1991) Childhood obsessive-compulsive disorder and cingulate epilepsy. *Biol. Psychiatry*, 30: 1049–1055.

Llinas, R. and Ribary, U. (1993) Coherent 40-Hz oscillation characterizes dream state in humans. *Proc. Natl. Acad. Sci. USA*, 90: 2078–2081.

Logothetis, N.K. and Schall, J.D. (1989) Neuronal correlates of subjective visual perception. *Science*, 245: 761–763.

Malloy, P., Cimino, C. and Westlake, R. (1992) Differential diagnosis of primary and secondary Capgras delusions. *Neuropsychiatry Neurophysiol. Behav. Neurol.*, 5: 83–96.

Mayberg, H.S. (1997) Limbic-cortical dysregulation: a proposed model of depression. *J. Neuropsych. Clin. Neurosci.*, 9: 471–481.

Mazoyer, B.M., Tzourio, N., Frak, V., Syrota, A., Murayama, N., Levrier, O., Salamon, G., Dehaene, S., Cohen, L. and Mehler, J. (1993) The cortical representation of speech. *J. Cog. Neurosci.*, 5: 467–469.

Nielson, J.M. and Jacobs, L.L. (1951) Bilateral lesions of the anterior cingulate gyri. *Bull. Los Angeles Neurol. Soc.*, 16: 231–238.

Olson, C.R., Musil, S.Y. and Goldberg, M.E. (1993) Posterior cingulate cortex and visuospatial cognition: Properties of single neurons in the behaving monkey. In: B.A. Vogt and M. Gabriel (Eds.), *Neurobiology of Cingulate Cortex and Limbic Thalamus*, Birkhäuser, Boston, pp. 366–380.

Pardo, J.V., Pardo, P.J., Janer, K.W. and Raichle, M.E. (1990) The anterior cingulate cortex mediates processing selection in the Stroop attentional conflict paradigm. *Proc. Natl. Acad. Sci. USA*, 87: 256–259.

Raichle, M.E., Fiez, J.A., Videen, T.O., MacLeod, A.-M.K., Pardo, J.V., Fox, P.T. and Peterson, S.E. (1994) Practice-related changes in human brain functional anatomy during non-motor learning. *Cereb. Cort.*, 4: 8–26.

Rainville, P., Duncan, G.H., Price, D.D., Carrier, B. and Bushnell, M.C. (1997) Pain affect encoded in human anterior cingulate but not somatosensory cortex. *Science*, 277: 968–971.

Rizzolatti, G., Matelli, M. and Pavesi, G. (1983) Deficits in attention and movement following the removal of postarcuate (area 6) and prearcuate (area 8) cortex in macaque monkeys. *Brain*, 106: 655–673.

Ruff, R.L. and Volpe, B.T. (1981) Environmental reduplication associated with right frontal and parietal lobe injury. *J. Neurol. Neurosurg. Psychiatry*, 44: 382–386.

Schanberg, S.M. and Field, T. (1987) Sensory deprivation, stress, and supplemental stimulation in rat pup and preterm human neonates. *Child Dev.*, 58: 1431–1447.

Sejnowski, T.J. (1986) Open questions about computation in cerebral cortex. In: J.L. McClelland and D.E. Rummelhart (Eds.), *Parallel Distributed Processing*, MIT Press, Cambridge, pp. 372–389.

Signer, S.F. (1992) Psychosis in neurologic diseases: Capgras symptom and delusions of reduplication in neurologic disorders. *Neuropsychiatry Neuropsychol. Behav. Neurol.*, 5: 138–143.

Sikes, R.W. and Vogt, B.A. (1992) Nociceptive neurons in area 24 of rabbit cingulate cortex. *J. Neurophysiol.*, 68: 1720–1732.

Solomon, P. (1961) *Sensory Deprivation*, Harvard University Press, Cambridge.

Stuss, D.T. and Benson, D.F. (1984) Neuropsychological studies of the frontal lobes. *Psychol. Bull.*, 95: 3–28.

Svensson, P., Minoshima, S., Beydoun, A., Morrow, T.J. and Casey, K.L. (1997) Cerebral processing of acute skin and muscle pain in humans. *J. Neurophysiol.*, 78: 450–460.

Valenstein, E., Bowers, D., Verfaellie, M., Heilman, K.M., Day, A. and Watson, R.T. (1987) Retrosplenial amnesia. *Brain*, 110: 1631–1646.

Vogt, B.A. and Pandya, D.N. (1987) Cingulate cortex of rhesus monkey. II. Cortical afferents. *J. Comp. Neurol.*, 262: 271–289.

Vogt, B.A., Rosene, D.L. and Pandya, D.N. (1979) Thalamic and cortical afferents differentiate anterior from posterior cingulate cortex in the monkey. *Science*, 204: 205–207.

Vogt, B.A., Vogt, L.J., Nimchinsky, E.A. and Hof, P.R. (1997) Primate cingulate cortex chemoarchitecture and its disruption in Alzheimer's disease. In: F.E. Bloom, A. Björklund and T. Hökfelt (Eds.), *Handbook of Chemical Neuroanatomy*, Vol. 13: The Primate Nervous System, Part I, Elsevier Science B.V., Netherlands.