One of Twenty Questions for the Twenty-First Century: How Do Brain Regions Interact and Integrate Information?

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What new insights will the twenty-first century bring to our understanding of how the brain supports cognition? At least one fundamental issue that will challenge scientists is uncovering the means by which the brain works as a cohesive and integrated processor to support mental functioning. The prevailing model today is that of localization of function, in which discrete functions are performed by distinct brain regions. Support for this perspective has been accumulating for at least a century, with the recent explosion in neuroimaging studies only reinforcing such a view. For example, neuroimaging studies have confirmed findings from patient populations linking dorsolateral prefrontal regions to working memory, superior parietal regions to attentional functions, and medial temporal regions to the acquisition of new declarative memories. It is probably fair to say that a major contribution of twentieth-century science has been to recognize that cognition is fractionated into biologically distinct components and to move toward mapping the neural geography of psychological functioning.

Nonetheless, we still have very little knowledge about how the biologically localizable and separable components of cognition are "bound together" to produce everyday behaviors. Trying to remember where one might have left one's keys, for instance, probably involves some interaction between the frontal lobes (which help with the strategic aspects of memory retrieval) and the temporal lobes (which help with accessing stored memories). As another example, consider maneuvering through a traffic jam in downtown Chicago while trying to ignore distracting music from the radio, honking horns and a back seat driver. This daunting task most likely requires interactions between the parietal lobes, which encode the spatial positions

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of objects in the environment such as other cars on the road, and the frontal lobes, which aid in keeping one's attentional "set" on the road rather than on the backseat driver.

Fortunately, there are already some hints as to how processing between different brain areas is bound. Studies examining the firing patterns of single cells suggest that temporally synchronous neuronal firing can bind the processing occurring in a number of discrete brain regions to create a larger functional unit. For example, neurons in different regions of the visual cortex fire in phase with one another if they are responding to the same object, but not if they are responding to different objects (Engel, Konig, Kreiter, Schillen, & Singer, 1992). On a larger scale, the joint use of transcranial magnetic stimulation (TMS) and PET is also providing insight into functional connectivity between brain regions. TMS disrupts the functioning of a relatively circumscribed region of neurons. When PET recordings are made following TMS to a particular brain region, patterns of deactivation in other brain areas that were not stimulated can suggest functional relationships between the stimulated and nonstimulated regions (Paus, Jech, Thompson, Comeau, Peters, & Evans, 1997).

Despite these clues, however, we are currently impoverished in regard to computational models that would enrich our understanding of interactions between brain areas. Although some models are being employed (Horwitz, Tagamets, & McIntosh, 1999), they have limitations. For example, path analysis utilizes correlation matrices to make statistical predictions about which variables are having significant effects on other variables. When applied to PET data, such models have been used to make inferences about which brain regions significantly affect other brain regions. A major constraint of such models, however, is that they require researchers to make assumptions not only about the brain regions that interact with one another, but also about the direction in which information flows between those regions. Such assumptions may not always be warranted. For example, although we think of primary sensory areas as feeding into secondary sensory areas, recent findings of attentional gating in primary sensory regions suggest feedback from higher to lower order areas.

Understanding interactions between brain regions is also complicated because the outcomes of such interactions are likely to be much more than the sum of their parts. Even when separating the brain into one of its simplest divisions—that of the left and the right hemispheres—there is clear evidence that the outcome of interaction between brain regions cannot always be predicted by the functioning of each brain region in isolation. For example, manipulations that affect neither the processing of the left hemisphere nor that of the right, nonetheless affect the processing of both hemispheres when they interact (Banich & Karol, 1992). Hence, an understanding of the behavior of brain regions as functional parts of a network requires more than an understanding of how individual brain regions behave in isolation.

Also complicating matters is evidence that interactions between brain regions are not static and can vary with task demands. Consonant with the findings from single-cell recording studies discussed earlier, certain conditions promote "binding" of processing between the hemispheres, while others do not. The degree of binding appears to be driven by the degree to which task demands place a heavy processing load upon the brain. When tasks are computationally simple, a single hemisphere working in isolation performs better than both hemispheres working together. This effect probably occurs because a single hemisphere has the processing capacity to support performance by itself and the overhead entailed by communication between the hemispheres is deleterious to task performance. On the other hand, when tasks are computationally complex, two hemispheres working together are better than one. Under these conditions, the gain in computational power afforded by a division of processing across two somewhat independent processors outweighs the costs of coordinating their interaction (Belger & Banich, 1998). What is most interesting about this phenomenon is that the hemispheres can adaptively change their mode of processing, decoupling when tasks are relatively simple and coupling when they are more computationally complex (Weissman & Banich, in press). Therefore, to understand how interactions between brain regions contribute to behavior will require that scientists consider that such interactions are dynamic and change with task demands.

What tools exist that are likely to provide answers to these questions? There is probably no single magical technique that will suffice. Some newly emerging methods such as event-related optical signal (EROS) measures may play an important role because they provide in a single measure a combination of good spatial and temporal resolution (Gratton & Fabiani, 1998). The pairings of more conventional measures with high spatial resolution, such as fMRI, and those with high temporal resolution, such as ERPs and MEG, may also play a large role. In the end, it will probably be a convergence of empirical, computational, and theoretical methods that will provide an answer to this mystery.

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