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# Brain Imaging and its impact on the development of Cognitive Science

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## Abstract

This symposium will address the new data and challenges presented by recent advances in brain imaging methodology. It will include tutorials on the available techniques: Positron Emission Topography (PET), Functional Magnetic Resonance Imaging (fMRI) and combined fMRI & high density Evoked Response Potentials (ERP). The impact of these techniques on the physiological interpretation of human working memory will be illustrated.

In the last five years there have been major advances in brain imaging methodology that provide the ability to look into the brain to identify the biological processes underlying cognition. Non-invasive techniques now allow tracking of neural activity by monitoring blood flow (PET, fMRI), specific chemical reactions (PET) and high speed electrical changes (ERP). The combinations of all of these techniques allow tracking of: the size and extent of processing with millimeter resolution, the nature of some of the chemical reactions, and the time course of the network cortical activity. Availability and limitations of each methodology will be discussed. Temporal resolution of fMRI is in the seconds range. By combining techniques we can create millimeter and millisecond maps of cortical function detailing the biological network interactions. The implications of such maps to the understanding of network cognitive processing will be commented upon. There will be five speakers and a panel discussion. Abstracts of the five talks are presented below.

**PET mapping activity and chemistry of cognitive function.** Cameron S. Carter (Western Psychiatric Institute & Clinic University of Pittsburgh) & Mark Mintun (University of Pittsburgh Medical Center).

Positron emission tomography, or PET, allows the in vivo human brain imaging of a variety of regional physiological variables. While cerebral blood flow and cerebral metabolic rate of glucose are the most common measurements made, more complex studies to quantitative the distribution of various receptors, the occupancy of receptors with neurotransmitters, and the rate of synthesis and release of neurotransmitters are increasingly common. An understanding of PET methodology and its limitations and potential applications requires an understanding of the three basic components of positron emission tomography. The first component involves the instrumentation required for imaging the radioactivity distribution within the brain. The basic principles of coincidence detection, which makes PET unique compared to other in vivo radioisotope imaging, will be presented. The dramatic impact of the recently developed three-dimensional acquisition schemes will also be reviewed. The second component of PET is radiochemistry. The principles and limitations of using radiotracers to probe regional neurochemistry and brain function will be presented. Finally, the study design and data analysis component which allows the PET measurements of radioactivity to be interpreted in physiologic terms will be introduced. Focus will be on studies to detect regional brain changes to cognitive task and drug intervention. This methodology will be contrasted with the techniques required to quantitate receptor physiology.

**Functional MRI: Methods and Applications.** Keith R. Thulborn (MR Research Center, University of Pittsburgh Medical Center).

The use of functional MRI to probe the hemodynamic response of the human brain to changing neuronal activity during cognitive processing is a promising tool for cognitive neuroscience. To reach its full potential, the MRI technology must be integrated with different

neuropsychological methodology. This requires an interdisciplinary team of investigators and the opportunity to design optimally the technology for this application. The newly instituted MR Research Program at the University of Pittsburgh Medical Center has provided this environment. The two MR scanners at 1.5 and 3.0 Tesla have been designed for fMRI at high spatial and temporal resolution. The routine performance of high quality fMRI studies has been achieved through the use of a customized control system for presentation of audiovisual stimuli in concert with image acquisition, physiological monitoring and task performance measures. This system will be described, and results of its use in probing various sensory and cognitive functions will be described.

**ERP and fMRI multi-modality constraints of activity - Providing temporal as well as spatial data on cognitive function.** Michael Worden, Walter Schneider (University of Pittsburgh)

High-Density Event-Related Potential (HD-ERP) recording provides excellent temporal information (in the 10 ms range) indexing cortical information processing but is limited in the spatial information which it supplies. Functional Magnetic Resonance Imaging (fMRI) provides high-resolution spatial information (approximately 1 mm in-plane resolution) about active brain areas but little information about the time course of activity in these areas. We combine these techniques such that the strengths of one technique constrain the shortcomings of the other. We use scalp electrical data to determine the time-courses of activation for the functional regions identified with fMRI. Using a multi-frame visual target-search paradigm, evoked potentials are recorded using a sixty-two channel ERP recording array. Discrete areas of cortical activation are identified using fMRI scanning on a conventional 1.5 Tesla MRI scanner while the subject performs the identical paradigm. This provides information on the number of active generators as well as detailed anatomical information about the configuration and orientation of the generators. The areas of cortical activation determined with fMRI are used to model the potential fields which are recorded under the same paradigm using HD-ERP. Electrode locations and skull landmarks are digitized for each subject to permit coregistration of the ERP data with the fMRI data. The analysis includes an assessment of the goodness-of-fit of forward-solution models for early visual components constrained by fMRI-defined areas of activation. Using the combined techniques we measure human attentional processing.

**PET studies of verbal working memory** Edward E. Smith, John Jonides, and Robert Koeppel (University of Michigan).

Subjects performed various verbal working memory tasks while being scanned. Our results indicate that verbal working memory contains two components: a storage component that is partly mediated by structures in left-hemisphere posterior parietal cortex, and a rehearsal component that is mediated by structures in frontal cortex that are known to be involved in explicit speech, including, among others, Broca's area.

**Functional MRI Studies of Working Memory and Prefrontal Cortex** Jonathan D. Cohen (Carnegie Mellon University & Western Psychiatric Institute & Clinic University of Pittsburgh) & Todd S. Braver (Carnegie Mellon University).

Prefrontal cortex (PFC) has long been implicated in a variety of higher cognitive functions, including working memory. In this presentation, we describe a series of studies using fMRI to examine the role of PFC in working memory. All studies used a sequential letter memory task, which required that subjects continually update and maintain information about the identity and sequential order of letter stimuli. The first three studies established: a) the ability of fMRI to detect activation of PFC during this task; b) the comparability of these findings to those using a different neuroimaging method (PET); and c) the test-retest stability of findings within individual subjects. The fourth experiment parametrically manipulated memory load, demonstrating a monotonic increase in the area and intensity of activation as a function of load. The final experiment varied the type of information that had to be maintained in working memory (letter identity vs. spatial location), in an effort to determine whether representations are supported by different regions of prefrontal cortex. Taken together, these studies demonstrate the usefulness of fMRI for studying the neural basis of higher cognitive processes and, in particular, provide new, more detailed evidence concerning the involvement of PFC in working memory.