fMRI references


The successful use of functional magnetic resonance imaging (fMRI) as a way of visualizing cortical function depends largely on the important relationships between the signal observed and the underlying neuronal activity that it is believed to represent. Currently, a relatively direct correlation seems to be favoured between fMRI signals and population synaptic activity (including inhibitory and excitatory activity), with a secondary and potentially more variable correlation with cellular action potentials.


Functional neuroimaging represents an area of brain imaging that has undergone tremendous advancements in the last decade. It is now possible to design experiments that elucidate the functional interplay between brain regions that give rise to specific human cognitive processes. Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) form the core technologies that have allowed such studies. This article reviews the basis of these techniques, their strengths and limitations, the underlying neurophysiology, and the future of functional neuroimaging.


Functional magnetic resonance imaging (fMRI) can provide maps of brain activation with millimeter spatial resolution but is limited in its temporal resolution to the order of seconds. Here, we describe a technique that combines structural and functional MRI with magnetoencephalography (MEG) to obtain spatiotemporal maps of human brain activity with millisecond temporal resolution. This new technique was used to obtain dynamic statistical parametric maps of cortical activity during semantic processing of visually presented words. An initial wave of activity was found to spread rapidly from occipital visual cortex to temporal, parietal, and frontal areas within 185 ms, with a high degree of temporal overlap between different areas. Repetition effects were observed in many of the same areas following this initial wave of activation, providing evidence for the involvement of feedback mechanisms in repetition priming.

Eyeblink conditioning has been used as a model for studying aging. Humans show learning deficits in this task after age 40. Some brain regions altered by aging are also involved in eyeblink conditioning. To assess age-dependent changes in learning-related brain circuits, we used BOLD contrast fMRI to quantify local perfusion changes during acquisition. We tested 20, 40, 60 and 80 yr old human subjects. Eyeblink conditioning used a 150 ms corneal airpuff (4.5 psi) US. A pure tone (80 dB, 1 kHz, 100 ms) CS was delivered binaurally through pneumatic headphones. A novel remote fiber optic eyeblink detector monitored responses, with all conditioning occurring inside the magnet. Pseudoconditioning used 60 trials, with the CS alone or US alone alternated pseudorandomly, with intertrial intervals (ITIs) of 18-22 s. Trace conditioning used 60 trials of the CS followed after a 500 ms interstimulus interval by the US, with 18-22 s ITIs. Images were obtained from a 1.5T GE NV/i MRI system. We obtained 16-18 coronal TI slices from frontal to occipital pole, ~10 mm in thickness. Multiple EPI volumes (gradient echo, TE/TR=45/2000, FOV=24 cm, 64X64) were taken during and for 16-20 s after trials at the same locales. Volumes were co-registered for motion correction. Our ITIs permitted nine to eleven 2 s T2* (BOLD) images to be collected per trial, allowing analyses of all hemodynamic responses. After subtraction of CS or US alone signals, analyses of multiple regions were carried out, in blocks of 5 trials each, looking for responses unique to associative learning. Results showed increased blood flow in the cerebellum, hippocampus and multiple cortical regions during conditioning, with some age-dependent changes. Implications for future work will be discussed.


Eyeblink conditioning has been used in studies of brain aging and its relation to altered neuronal and behavioral plasticity. All species tested exhibit age-dependent deficits in acquiring this associative learning task, with human deficits observed at ages >40. We used BOLD contrast fMRI to quantify age-dependent perfusion changes in multiple learning phases. Parametric assessments were made of the time course of BOLD changes, and of their relation to stimulus presentation, stimulus pairing, and learning across multiple ages. From normal 20-80 year old volunteers, we obtained 16-18 coronal T1 ~10 mm slices from frontal to occipital pole with a 1.5T GE NV/i MRI. All testing occurred during
functional scanning. Eyeblink conditioning used 150 ms left corneal airpuff (5 psi) USs and 100 ms binaural tone (80 dB, 1KHz) CSs, delivered via pneumatic headphones. Our fiber optic detector monitored blink responses in real-time. Pseudoconditioning trials (random sequences of interspersed CS or US trials, 30 each, ITI average 16s) were followed by 60 trace conditioning trials (500 ms ISI, average ITI 16 s). Multiple EPI volumes (gradient echo, TE/TR=45/2000, FOV=24 cm, 64x64) were taken, and coregistered with the T1 images for motion correction. Age-, stimulus-, and learning-related changes in blood flow were detected in cortical, subcortical, and cerebellar areas. The time course of these changes for different trial types were characterized, and implications for design of event-related learning studies are discussed.


A distributed network of brain regions supports memory retrieval in humans, but little is known about the functional interactions between areas within this system. During functional magnetic resonance imaging (fMRI), subjects retrieved real-world memories: autobiographical events, public events, autobiographical facts, and general knowledge. A common memory retrieval network was found to support all memory types. However, examination of the correlations (i.e., effective connectivity) between the activity of brain regions within the temporal lobe revealed significant changes dependent on the type of memory being retrieved. Medially, effective connectivity between the parahippocampal cortex and hippocampus increased for recollection of autobiographical events relative to other memory types. Laterally, effective connectivity between the middle temporal gyrus and temporal pole increased during retrieval of general knowledge and public events. The memory types that dissociate the common system into its subsystems correspond to those that typically distinguish between patients at initial phases of Alzheimer’s disease or semantic dementia. This approach, therefore, opens the door to new lines of research into memory degeneration, capitalizing on the functional integration of different memory-involved regions. Indeed, the ability to examine interregional interactions may have important diagnostic and prognostic implications.

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The intrinsic flexibility of functional magnetic resonance imaging has allowed ever more innovative neuroscience applications. New acquisition and analysis techniques have contributed to improvements in detection sensitivity, as well as spatial and temporal resolution. Furthermore, by considering the dynamic evolution of the active brain areas in a network, computational models are making the first steps towards linking brain and mind.


We combined fMRI and EEG recording to study the neurophysiological responses associated with auditory stimulation across the sleep-wake cycle. We found that presentation of auditory stimuli produces bilateral activation in auditory cortex, thalamus, and caudate during both wakefulness and nonrapid eye movement (NREM) sleep. However, the left parietal and, bilaterally, the prefrontal and cingulate cortices and the thalamus were less activated during NREM sleep.

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compared to wakefulness. These areas may play a role in the further processing of sensory information required to achieve conscious perception during wakefulness. Finally, during NREM sleep, the left amygdala and the left prefrontal cortex were more activated by stimuli having special affective significance than by neutral stimuli. These data suggests that the sleeping brain can process auditory stimuli and detect meaningful events.


The phenomenon of temporally graded retrograde amnesia (loss of information acquired before the onset of amnesia) suggests that the hippocampus, and possibly other medial temporal lobe (MTL) structures, have a time-limited role in memory. In three experiments, we made a first attempt to use fMRI to assess activity in the hippocampal region (the CA fields of the hippocampus, the dentate gyrus, and the subiculum) and the adjacent parahippocampal gyrus (parahippocampal, entorhinal, and perirhinal cortices) during recognition memory testing as a function of study-test interval. Experiment 1 (n = 5) demonstrated activity in the hippocampal region and parahippocampal gyrus for targets relative to foils during recognition memory performance following a single study-test delay of about one-half hour. In Experiment 2, 15 participants studied line drawings at each of three different times prior to scanning: one-half hour, 1 day, and 1 week. fMRI data were then collected during recognition memory testing, using targets from all three delays and foils. While an overall effect of targets vs. foils was found in both the hippocampal region and the parahippocampal gyrus, there was no effect of study-test interval on target activity. In Experiment 3 (n = 13), behavioral performance (reaction time and accuracy) was equated across the three delays. Again, no effect of study-test interval was observed. It is possible that the time span sampled in our study (one-half hour to 1 week) was too short to observe changes in activity. Alternatively, activity in the MTL during memory testing may occur even when these structures are not necessary for retrieval.


The importance of the medial temporal lobe in memory has been studied extensively at the neuronal, neural ensemble, and systems level. In this report, we discuss recent systems level neuroimaging results in relation to neurophysiological
studies of the hippocampus and related structures within the medial temporal lobe. By combining our knowledge across the cellular and systems levels we sought to gain theoretical insight and a better understanding of the function of the hippocampus and related medial temporal lobe structures. The integration of information from studies carried out at the cellular and neural ensemble level with studies at the systems level is difficult because of the vast differences in spatial and temporal resolution of the different research methodologies, differences in neuroanatomy across species, and differences in the types of behavioral and cognitive paradigms used in rat, nonhuman primate, and human studies. Despite these methodological and species-related differences, the neurophysiological studies offer insight into many of the questions raised by recent neuroimaging studies. For instance, there is physiological evidence that suggests that the hippocampal memory system is functionally heterogeneous, which may explain some of the discrepancies in the location and extent of activation reported by different imaging studies of the medial temporal lobe. In addition, we describe recent computational models of the hippocampus which may be useful for bridging the gap between neurophysiological and neuroimaging data.