Basic Neuroscience: fMRI Studies of Sensory Systems

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Highlights.

- The sensory pathway is topographically organized.
- Feed forward and feedback mechanisms act between relays.
- These processes are spatially segregated.
- High-resolution imaging is a window in the basic principles of human perception and behavior.

Target Audience	Neuroscience.
Objective	Highlight the advance in in vivo functional imaging through the combination of high field/ high-resolution MRI measures and computational models of perception.

Sensory information travels from the periphery (e.g. eye, cochlea) through the thalamus and reaches dedicated cortical areas. This dedicated circuitry allows us to interpret the physical world and react appropriately according to it. At each stage the sensory pathway neurons are with similar "receptive fields" (i.e. preference to a specific portion of the sensory input) are topographically organized. In the cortex neurons with similar receptive fields are organized in cortical columns. Connections relay information from lower to higher-level stages. This feed forward "stream" is shaped by the tuning properties of neurons. Neuronal populations at higher levels have generally larger and more complex receptive fields. At the same time feedback connections relay information in an opposite direction adjusting neuronal tuning depending on behavioural relevance. Importantly, in both sub-cortical and cortical areas feed forward and feedback processing is spatially segregated. At cortical level, for example, different cortical laminae (layers) are characterized by a different distribution of feed forward and feedback connections.

This level of description of sensory processing comes mostly from invasive electrophysiological studies in animals or post mortem human studies of brain structure. These investigations have served as the backbone to the study of human brain function in-vivo using functional magnetic resonance imaging (fMRI), despite the difference in spatial scale between them (i.e. from single neurons to 3 mm isotropic acquisitions of conventional fMRI investigations). Since its introduction 20 years ago (1,2), fMRI has evolved into the most commonly used methodology for mapping brain function, particularly in humans. The ability to non-invasively monitor processes related to brain function with high degrees of spatial and temporal precision has proven to be an invaluable tool for neuroscience. The last decade has seen the development of high field imaging scanners. A great technological effort has allowed their steady introduction in the neuroimaging field. From few pioneering applications (3), high field fMRI has now become a fundamental tool for the investigation of the basic architecture of sensory (and non-sensory) brain structures. Higher field strengths translate into higher signal to noise ratios (4). Further, the BOLD contrast (the basis of functional imaging) increases supra-linearly with field strength (5,6). These advantages translate into the possibility of acquiring images with higher spatial resolution. High spatial resolution alone is not sufficient to achieve higher spatial specificity, as the BOLD response is ultimately limited by the underlying vascular contributions and their spatial point spread function (7). Standard T_2*

based BOLD contrast, which is used in the vast majority of fMRI studies (gradient-echo echo-planar imaging [GE-EPI]), is sensitive to both micro and macro-vasculature components at high magnetic fields (7-12). As a result, large draining veins (penetrating the cortex orthogonally or lying on top of the grey matter surface) affect the BOLD signal acquired with GE-EPI (8,9,12-18). On the other hand, T_2 weighted (spin echo echo-planar imaging [SE-EPI]) is substantially less sensitive to large vein effects (19,20).

Independent of the specific acquisition technique, high field functional imaging has allowed the investigation of human functional topographies in sub-cortical and cortical structures in-vivo at unprecedented spatial scales. Columnar organizations in primary (19,21) and non primary (22) visual cortex, layer dependent functional responses (14-16,18,23), layer specific task dependent modulations of visual (24) areas, layer dependent functional connections between visual cortical processing relays, functional topographies of sub-cortical areas (25) are some of the applications that showcase the potential of high field functional imaging as a fundamental tool to bridge the gap between in-vivo investigations in humans and invasive electrophysiology in animals. Together with advances in analysis methods that allow the link between computational models and in-vivo measures of brain function (26-28), mapping of population receptive fields at high fields (29,30) and their modulation and functional connectivity across stages of the perceptual pathway represents an opportunity to study human brain function in ecologically valid settings (i.e. the use of more naturalistic stimuli).

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