

High-resolution functional MRI for mapping cortical microcircuits in humans.

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Introduction

High-resolution functional magnetic resonance imaging (fMRI) has opened new frontiers in the study of human brain organization by enabling the mapping of cortical microcircuits with unprecedented detail. Traditional fMRI, with spatial resolutions of around 2–3 millimeters, has been instrumental in revealing large-scale brain networks but has lacked the precision needed to resolve fine-grained functional architecture within cortical columns and layers. Recent advances in ultra-high-field MRI systems, such as 7 Tesla and beyond, along with refined acquisition sequences, have pushed spatial resolution into the submillimeter range. This leap in resolution allows researchers to investigate laminar-specific activation patterns and columnar organization in vivo, providing critical insights into the fundamental processing units of the human cortex. By capturing functional activity at the mesoscopic scale, high-resolution fMRI bridges the gap between macroscopic imaging and microscopic cellular recordings, offering a powerful tool for linking neural computations to complex human behavior [1].

A major advantage of high-resolution fMRI lies in its ability to perform layer-specific analyses, which can

reveal the directionality of information flow within cortical microcircuits. The cerebral cortex is organized into distinct laminae, each with unique inputs, outputs, and computational roles. For example, feedforward sensory information typically enters layer 4, while feedback projections often target superficial and deep layers. With high-resolution acquisitions, it is possible to differentiate activation patterns across these layers, providing clues about whether a given task engages primarily feedforward or feedback processing. This capability is particularly valuable for studying cognitive functions such as attention, working memory, and sensory integration, as well as for investigating how these processes are disrupted in neurological and psychiatric disorders. The ability to probe laminar-specific activity noninvasively in humans represents a major methodological advance, offering a window into circuit-level dynamics that were once accessible only through invasive animal studies [2].

Columnar organization is another key target of high-resolution fMRI. Many cortical areas, including the primary visual cortex, auditory cortex, and somatosensory cortex, are organized into functional columns that process specific stimulus attributes such as orientation, frequency, or tactile location. Traditional fMRI methods blur these fine-scale

patterns due to limited spatial resolution and partial volume effects, making it difficult to study their functional role in detail. High-resolution imaging, particularly when combined with advanced analysis methods like multivoxel pattern analysis (MVPA), can detect subtle columnar activation differences, allowing researchers to decode stimulus features at a level of precision previously thought unattainable in humans. This capability not only deepens our understanding of sensory processing but also provides a platform for studying how microcircuit-level coding supports higher-order cognition and perception [3].

Technical innovations have been critical for achieving the performance required for high-resolution fMRI. Ultra-high-field magnets increase the signal-to-noise ratio, enabling smaller voxel sizes without sacrificing sensitivity. Parallel imaging techniques and simultaneous multislice acquisition further accelerate data collection, reducing the impact of subject motion and physiological noise. Specialized pulse sequences, such as three-dimensional gradient-echo and spin-echo echo-planar imaging, have been optimized for laminar and columnar resolution while minimizing signal distortions caused by magnetic field inhomogeneities. In addition, sophisticated preprocessing pipelines have been developed to correct for motion, distortion, and signal bias across cortical depths. These advancements collectively enable the reliable acquisition and analysis of high-resolution fMRI data, making the study of cortical microcircuits a practical reality rather than a technical aspiration [4].

Despite these advances, high-resolution fMRI still faces significant challenges. Ultra-high-field imaging increases susceptibility to artifacts, particularly in regions near air-tissue interfaces such as the orbitofrontal cortex and temporal lobes. Motion artifacts become more problematic as voxel size decreases, requiring strict head stabilization and advanced motion correction algorithms. Physiological noise from respiration and cardiac pulsation can mimic or obscure laminar-specific

activation patterns, making it essential to incorporate physiological monitoring and noise modeling into the analysis. Another challenge lies in the interpretation of high-resolution BOLD signals, which are influenced by vascular architecture in addition to neuronal activity. Disentangling vascular from neural contributions is a key area of ongoing research, with approaches such as vascular space occupancy (VASO) imaging and calibrated fMRI offering promising solutions. Finally, the increased cost, limited availability, and specialized expertise required for ultra-high-field imaging remain barriers to widespread adoption, though these limitations are gradually diminishing as the technology matures [5].

Conclusion

High-resolution functional MRI represents a transformative advance in neuroimaging, enabling the *in vivo* study of cortical microcircuits with unprecedented spatial precision. By resolving laminar- and columnar-scale activation patterns, this technology provides critical insights into the directionality of information flow and the fine-scale functional architecture underlying perception, cognition, and behavior. Technical innovations in hardware, acquisition, and analysis have made it possible to capture these details reliably, while ongoing methodological refinements are addressing the remaining challenges of artifact reduction, noise suppression, and physiological interpretation. As ultra-high-field imaging becomes more accessible, high-resolution fMRI will play an increasingly central role in bridging cellular-level neuroscience with systems-level understanding in humans, offering a powerful tool for both basic research and clinical translation.

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