## **Fifteen Years of Functional MRI**

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It's been about 15 years since the first successful functional MRI (fMRI) experiments were performed. Since then, the field of functional neuroimaging has experienced an explosive growth as neuroscientists had access to a new spatial and temporal niche for exploring brain function.

How exactly did fMRI emerge and grow so rapidly? A serendipitous combination of five factors was essential. These factors include: 1. The unique characteristics of red blood cells: They change their magnetic susceptibility depending on whether or not they are bound to oxygen. Fully oxygenated blood has the same susceptibility as body tissue. Deoxygenated blood is less diamagnetic than tissue - setting up microscopic field perturbations, leading to MR relaxation alterations. 2. The unique characteristics of brain activation related hemodynamic changes: With activation, blood flow locally increases, and despite an increase in the metabolic, an apparent overabundance of oxygenated blood is delivered, resulting in a net decrease in the amount of deoxyhemoglobin. 3. The spatial scale of brain organization: It is serendipitous that the brain is organized such that modular functional units are on a similar spatial scale as MR voxel size. While brain is organized across many spatial scales, the spatial scale of millimeters to centimeters appears to be particularly informative with regard to functional organization. 4. Echo planar imaging (EPI): EPI is technically challenging because of the requirement for precise control of large, rapidly changing magnetic fields. EPI emerged only in the early 90's. The temporal stability of EPI is an order of magnitude greater than uncorrected standard multi-shot imaging, allowing fMRI magnitude (about 1%) signal changes to be detected. 5. The prevalence of MRI scanners: Lastly, during the early 90's the overwhelming clinical utility of MRI led to a proliferation of scanners. In essence, every hospital therefore had the potential to perform fMRI. During the later part of the 90's, this potential for fMRI was realized as these clinical scanners were typically used during the daytime for clinical anatomic imaging, and in the evening for fMRI research.

All of these variables came together in a serendipitous confluence that resulted in the explosive growth of fMRI research in the past 15 years. Over these years, the co-development of fMRI technology, methodology, interpretation, and applications have helped to shape the landscape of neuroimaging. In this lecture, I will discuss in more detail the five factors that led to the discovery and growth of fMRI as well as some of the milestones associated with each of the four co-developing components. I will also discuss some of the more recent advances as well as the ultimate spatial, temporal, interpretive, and practical limits of fMRI.