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## **Manganese-Enhanced MRI for Functional Imaging of Freely Moving Animals**

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Advanced in vivo methods that enable the imaging of neural activity across the entire brain are crucial for understanding how information is processed during specific behaviors. One such method is manganese-enhanced magnetic resonance imaging (MEMRI), which allows the time-integration of neural activity in freely moving animals. MEMRI utilizes Mn<sup>2+</sup>, a paramagnetic ion that enhances MRI contrast, and serves as a surrogate marker for Ca<sup>2+</sup> influx, which accumulates in neurons in an activity-dependent manner.

One major advantage of MEMRI is that it utilizes a residual and integrative contrast that can be highlighted via MRI after the animal has exhibited its specific behavior under natural conditions. This is a significant improvement over BOLD functional MRI (fMRI), which is primarily used in humans but relies on momentary hemodynamic contrast that lasts only a few tens of seconds. Thus, BOLD fMRI requires the animal to be stimulated during the MRI experiment, often under anesthesia.

Examples of high-field MEMRI will be discussed, demonstrating the potential of this approach for studying rat behaviors. Key considerations will be discussed, including the methods for administering Mn and detecting differences in brain activity among groups of animals exhibiting contrasted behaviors. By exploring these critical points, we can better understand how to utilize MEMRI to investigate neural activity in rats and gain insights into the underlying brain mechanisms governing behavior and nutrition.