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(G*) Multi-modal PET-MR imaging of the selective activation of serotonergic neurons in living rodent brains with DREADD technology

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The main advantage of hybrid PET-MR imaging systems is the ability to correlate anatomical with metabolic information directly. The bulk of commercially available PET-MR systems are quite large and expensive and mostly used on humans rather than for preclinical animal studies. This has led to a gap of knowledge in PET-MR imaging of small animal models used in preclinical research. Our work takes advantage of a new imaging system developed by Cubresa called 'NuPET'. This device is a MR-compatible PET scanner placed around the subject while they are within the toroidal bore of a MR scanner. With this equipment we are attempting to demonstrate the selective activation of serotonergic neurons in living rodent brains. To specify which neurons are to be activated, we use Designed Receptors Exclusively Activated by Designer Drug (DREADD) technology. These DREADDs are designer G-protein-coupled receptors. Neurons at the site of a stereotactic injection are transfected with a viral vector containing the proteins necessary to force expression of DREADDs in genetically modified rats. These may then be activated by administering the designer drug clozapine-N-oxide (CNO). This technique allows for precise spatiotemporal control of receptor signaling in vivo. Over two experiments (N=5, N=2) we have attempted to image the effect of DREADDs-mediated excitation of 5-HT neurons in rats. Voxel-based analysis of the data thus far show no confirmed statistically significant differences between rats given saline and those given CNO. Numerous methodological issues have been discovered within the experimental design, and are being addressed for a new trial of the technique and technology.

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