Exploring Dopaminergic Pathways in the Brain Using Preclinical Pharmacological MRI

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Disruptions in neurotransmitter systems, including the dopaminergic system, occur in various neurological and neuropsychiatric disorders such as schizophrenia, addiction, and Parkinson's disease. Understanding how dopamine pathways function in the healthy brain and how they are altered in disease is essential for developing effective treatments.

In this project, we aim to establish a novel preclinical pharmacological MRI (phMRI) protocol to study the two main dopaminergic pathways: the direct and indirect pathways. phMRI represents a powerful non-invasive method that combines functional MRI with a pharmacological compound to study how the brain responds to the modulation of specific pathways. By analyzing changes in brain activity following the administration of drugs that selectively affect dopamine receptors in the direct and indirect pathways, we aim to map pathway-specific responses across the brain.

Using a 9.4T MRI system, we acquired whole-brain phMRI data (5 s/image, resolution = 0.3 mm) from anesthetized mice. Ten minutes prior to scanning, domperidone (intraperitoneal, i.p.) was given to minimize peripheral effects of the pharmacological compounds. After 15 min. of baseline scans, a drug mixture of either D1-receptor agonist and D2-receptor antagonist (to interrogate the direct pathway) or D2-receptor agonist and D1-receptor antagonist (to interrogate the indirect pathway) was injected as a bolus via an i.p. infusion line. The acquisition continued for an additional 51 min. to allow investigation of temporal pathway-specific changes.

PhMRI data are processed using Matlab R2021a and SPM12 and analyzed with a focus on key dopaminergic brain regions such as the caudate putamen, globus pallidus, and motor cortex.

Our goal is to apply this method first in healthy subjects and later in animal models for dopaminergic disorders to enhance our understanding of alterations in dopaminergic signaling and to guide the development of novel and effective therapies.