

Amphetamine pharmacMRI in the rat under isoflurane anesthesia

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Introduction

Direct pharmacMRI is a useful method to investigate the effects of psychogenic drugs on brain activity in vivo (McKie, 2005). We previously established localized changes in blood-oxygenation level dependent (BOLD) contrast in the rat brain following psychomimetic doses of ketamine in regions relevant to schizophrenia using direct pharmacMRI. To further investigate the effects of psychomimetic drugs on BOLD contrast we investigated d-amphetamine, a standard drug used in preclinical schizophrenia research.

Methods

Adult male rats were anaesthetized with isoflurane (1.5%) and placed in a small bore 7T horizontal superconducting magnet. BOLD sensitive T2*-weighted images were acquired using a gradient echo sequence. A 2.5 cm surface coil was used for excitation and detection. Eleven contiguous 1 mm thick axial slices were collected per volume. In total 72 volumes of 70 seconds were collected, with 18 volumes (20 minutes) baseline scans and 52 post-injection scans (63 minutes). Vehicle (0.9% saline) or d-amphetamine (1 mg/kg) was injected (s.c.) at the start of volume 19. Data were preprocessed and analyzed using a general linear model in SPM2. For each individual subject, averaged baseline values were subtracted from post-injection time which was divided into six time bins of 9 volumes each. Statistical group comparisons were made for each time-bin using a 2 sample t-test ($p < 0.05$ uncorrected).

Results

d-Amphetamine administration resulted in cortical activations, including the piriform, prefrontal, cingulate, sensory motor and temporal cortex. Subcortical areas activated included the septum, reticular and anterior thalamus. A few clusters with deactivations were detected, including the periaqueductal grey and deep mesencephalic nucleus. d-Amphetamine induced activations showed significant effects over time.

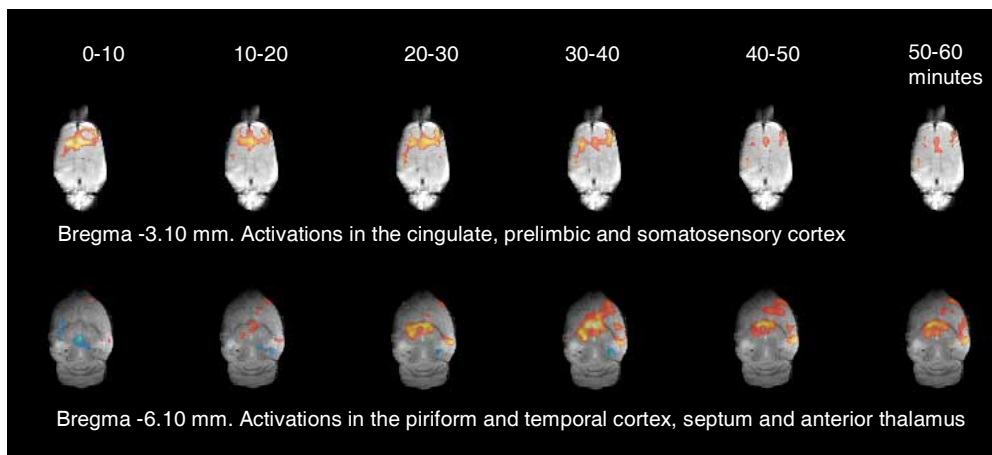


Figure 1a. Group T maps (amph-veh, $n=7$, $p < 0.05$ uncorrected), overlaid onto axial structural scans. From left to right are the six time intervals (10 min averages) shown after d-amphetamine administration. Activations are shown in red and deactivations in blue. T value range is set from 1.78 to 5.00.

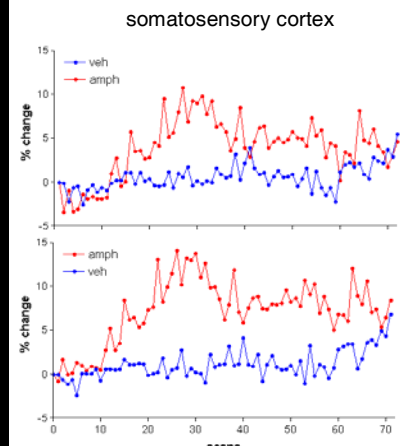


Figure 1b. Time course of selected voxels ($n=7$ each group) in the somatosensory cortex.

Discussion

This study demonstrates that d-amphetamine produces temporal and localized BOLD contrast changes in the rat brain under isoflurane anesthesia. Our study confirms a previous amphetamine pharmacMRI study in the rat (Dixon, 2005). However, we used a lower dose of d-amphetamine and used a different route of administration, which are more commonly used in preclinical schizophrenia research. Rat pharmacMRI at 7T offers novel ways to investigate preclinical models of schizophrenia and may help to understand the neurochemical basis of schizophrenia and psychosis.

References

1. McKie et al. (2005) *Psychopharmacology* 180(4):680-6
2. Dixon et al. (2005) *Neuropharmacology* 48(2):236-45

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