

MAPPING BRAIN ACTIVITY FOLLOWING GAMMA-HYDROXYBUTYRIC ACID ADMINISTRATION USING FUNCTIONAL MAGNETIC RESONANCE IMAGING IN RATS

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With its unique high temporal and spatial resolution functional MRI (fMRI) has recently emerged as powerful technique to detect changes in specific brain regions in response to pharmacological agents (1). Lately, we have utilized the blood oxygen level dependent (BOLD) fMRI method in order to investigate the effects of the recreational drug gamma-hydroxybutyric acid (GHB) on the rat brain reward system. Using a four-shot, gradient echo echo-planar imaging (EPI) sequence and a 9.4 Tesla scanner, we observed that systemic administration of GHB (50 mg/kg i.v.) determines regionally specific fMRI signal changes manifested as BOLD signal decreases (2). In particular, signal decrements were located within brain areas (such as prefrontal cortex, nucleus accumbens and dorsal striatum) rich in dopaminergic projections and known to play an important role in mediating both the rewarding, motivational and addicting properties of abused drugs. On these bases, the purpose of the present study was to use different fMRI techniques (BOLD and Cerebral Blood Volume, CBV) in order to establish a dose-response relationship for the functional responses observed after acute GHB administration, and to clarify the receptorial mechanisms underlying them. Specifically, experiments with a lower dose (25 mg/kg i.v.) of GHB are in progress, together with investigations aimed at getting further insight into GHB mechanism of action. In particular, we are comparing GHB effects on BOLD or CBV fMRI signals with those exerted by the GABAB receptor agonist baclofen, which possesses similar neuromodulatory actions (3, 4) and shows anti-craving properties both in humans and laboratory animals (5). Moreover, experiments are underway in order to verify whether a pretreatment with a GABAB antagonist is able to prevent GHB functional effects.

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