

## **Effects of lorazepam and scopolamine on encoding face-name associations: A pharmacologic fMRI trial**

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### **Introduction:**

Recent functional neuroimaging studies have reported robust activation in the hippocampus and related structures with memory paradigms, and a small number of studies have reported reduced activation in these regions in patients with memory impairment. We sought to test the hypothesis that pharmacologically induced memory impairments are associated with anatomically specific alterations in patterns of fMRI activation, using a face-name paired associated learning paradigm.

### **Methods:**

Ten right-handed, English speaking male subjects (ages 23-35) were scanned on 4 occasions, with a 2 week interval between each scanning session. Subjects were given intravenous saline placebo during the first and second scanning sessions, to test the reproducibility of the pattern of activation. During the third and fourth sessions, subjects were alternately given lorazepam 1 mg or scopolamine 0.4mg intravenously in a double-blind randomized cross-over design. We previously developed and validated 4 equivalent face-name pair stimulus sets, each containing 84 novel face-name pairs and 2 repeated face-name pairs, presented in blocks alternating with visual fixation. The stimulus sets were presented in random order. Scanning was performed during the encoding of the face-name associations, and subjects were tested immediately after scanning for face recognition, free recall for the names, and forced choice face-name association. Twelve anatomic regions of interest (ROI) were drawn on MPRAGE structural images for each individual subject and then registered to the functional data from each of the 4 scanning sessions. Reproducibility and drug effects were assessed comparing the number of significantly activated voxels within each anatomic ROI.

### **Results:**

Significant activation was observed in the striate, fusiform, parahippocampal, hippocampal, and dorsolateral prefrontal ROIs in both placebo sessions. The percentage of voxels activated within each of these regions showed no significant differences between the first and second placebo scans. With the administration of either lorazepam or scopolamine, a significant reduction in activation was observed in the right hippocampus and in bilateral fusiform regions ( $p < 0.05$  to  $p < 0.005$ , paired t-test), while other anatomic regions showed activation similar to placebo. Both lorazepam and scopolamine significantly impaired performance on the post-scan memory testing. Memory performance was significantly correlated with extent of activation in bilateral fusiform ROIs both across and within placebo/drug conditions.

### **Conclusions:**

Pharmacologic effects can be detected by fMRI in a reproducible experimental paradigm involving a paired associate memory task. Both lorazepam and scopolamine diminished activation in specific brain regions known to subservise this task. The reliability and validity of these data, using medications known to impair memory, suggests that fMRI may prove a useful tool in the screening of compounds being developed to enhance memory and treat cognitive impairment.