Supplementary Online Content


eAppendix. Supplemental material.
eFigure. Results of a post-hoc, region of interest analysis.

This supplementary material has been provided by the authors to give readers additional information about their work.
Supplemental Material

**Background**: The relevance of the anterior cingulate cortex (ACC) in mood disorders [1, 2] and the demonstration that activity in ACC can predict antidepressant treatment response (reviewed in [3]) suggest that a targeted ROI analysis designed to look at the ability of the ACC to predict response to scopolamine is appropriate. As no ACC region was identified in the whole brain analysis, a post-hoc ROI analysis was conducted with data from the 2 task components that produced significant results in the whole brain analysis (Encode and Test in the emotion WM task).

**Methods**: Post-hoc ROI analyses were conducted and limited to the ACC region (defined using AFNI[4]). The voxel level significance threshold for the correlations between treatment response to scopolamine and baseline BOLD responses for the encode and test components of the emotion WM task was defined at \( p< 0.05 \). A small volume correction then was applied.

**Results**: Overlapping areas in the pregenual (i.e., rostral) ACC were identified in the correlation analyses between treatment response magnitude and the BOLD response from the encode (fig S1a; center of mass coordinates based on Tailarach and Tourneaux[5] \((x,y,z) = 5.6, 41, -2.4\) and \(-7.6, 43, -4\)) and test (fig S1b; TT coordinates = -1, 41, -4) components of the emotion WM task. The observed positive correlations are opposite in direction to those seen in visual processing areas, thus showing that higher BOLD response at baseline is associated with greater treatment response. The extent of these correlations does not remain significant after applying the small volume correction (SVC) for multiple comparisons.
**Discussion:** The ACC is critically involved in mood disorders and activity levels in the ACC prior to or early in treatment can predict treatment response. The results here show the higher levels of task relevant activity at baseline predict subsequent treatment response to scopolamine. These clusters are located in the vicinity of regions identified in previous studies showing that neurophysiological activity is associated positively with the response to various antidepressant treatments (reviewed in [3]). While the correlations did not reach significance based on the SVC, the previous, highly replicated implications of the ACC renders these findings of interest.
References


Figure Legend

Figure S1. Results of a post-hoc, region of interest analysis are shown. Voxels within the anterior cingulate cortex that have correlations (voxel p< 0.05) between treatment response (change in MADRS) to scopolamine and baseline BOLD response to the encoding (A) and the test (B) component of the emotion working memory task are shown. The representative scatter plots and the best-fit lines also are presented.

BOLD= Blood oxygen level dependent
MADRS= Montgomery–Asberg Depression Rating Scale