Supplementary Online Content


eAppendix. Supplemental Materials
eReferences

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

Methods

Participants
While these are the same subjects and the pretreatment data is the same as that published in\(^1\), this is not a re-analysis of the same data. We have not reported on either the fMRI data during down-regulation of negative affect at 8 and 24 weeks or the HAMD data over the six month study\(^{1,4}\).

Image Analysis
Regarding multiple comparison correction, we have adopted such an approach to multiple comparison correction in several of our previous studies\(^ {1-3}\). Using the AlphaSim program as part of AFNI, this technique uses a cluster-size thresholding approach based on Monte Carlo simulation. With this technique, the overall family-wise error rate (FWE) is controlled by simulating null data sets with the same spatial autocorrelation as found in the residual images and creating a frequency distribution of different cluster sizes. Clusters with a size that exceeds the minimum cluster size corresponding to the a priori chosen FWE are retained for additional analysis. This cluster-based method of thresholding, analogous to cluster-based thresholding using Gaussian Random Field Theory\(^5\), is an alternative to voxel-based correction and is often more sensitive to activation when one can reasonably expect multiple contiguous activated voxels\(^6,7\).

Grey Matter Probability
For analyses of Grey Matter Probability (GMP), we used FSL’s FAST algorithm\(^8\) and controlled for GMP on a voxelwise basis.

Results
In order to address the question of whether changes in brain or symptomatology were related to the rate of change in SSRI treatment, we calculated a trajectory for each depressed patient for rate of change in medication dosage over the six-month trial. Including rate of change of antidepressant treatment in the regression equation did not attenuate the relationship between slope of DLPFC activity and HAMD trajectory (B=-11.61, t(18)=-2.97, \(p=0.008\)). Nor did it attenuate the relationship between slope of BA10 activity and HAMD trajectory (B=-12.20, t(18)=-3.41, \(p=0.003\)).

Discussion
A recent example of the power of the trajectory based approach is described in\(^9\). Using such approaches, Uher and colleagues examined the rates and trajectories of depression severity improvement following escitalopram or nortriptyline treatment. Whereas traditional approaches examining endpoints (using a last observation carried forward [LOCF] technique) and assessing “remission” or “response” favored escitalopram over nortriptyline, examining the symptom trajectories showed that individuals taking nortriptyline demonstrated more rapid reductions in depression symptom severity. Only examining baseline and endpoint data would have discarded the relevant data to examine response trajectory and would not have allowed for as rich an understanding of treatment response to these medications.
eReferences


4. Light SN, Heller AS, Johnstone T, et al. Reduced right ventrolateral prefrontal cortex activity while inhibiting positive affect is associated with improvement in hedonic capacity after 8 weeks of antidepressant treatment in major depressive disorder. *Biol Psychiatry.* Nov 15 2011;70(10):962-968.


