The Neural Mechanisms Underlying Problem-Focused Rumination in Depression

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Aims & Background

Aim. To examine neural correlates and mechanisms underlying autobiographical problem-solving deficits (APS) in major depressive disorder (MDD) that drive rumination.

Background

- MDD is marked by rumination, defined as repetitively focusing on one's emotions and problems[1] with the adaptive intent of understanding them and identifying possible solutions.[2-5] However, this process does not lead to the generation of solutions and may instead perpetuate ruminative processing.[7]
- We hypothesized that APS deficits may be driven by difficulties engaging the dorsomedial prefrontal cortex (DMPFC) which is thought to facilitate mental simulation of possible solutions to personal problems. We predicted that this failure occurs due to individuals with MDD failing to represent their problems in concrete terms.[8,9]
- In addition, we hypothesized that this failure would result in MDD individuals becoming stuck elaborating on aspects of their problems, reflected in greater activation in the precuneus,[10] and experiencing increased negative emotion, supported by the amygdala and right anterior insula.[11]

Methods

Sample

- 16 Unmediated Depressed ($M(SD)_{age}$= 25.4 ±7.3 , 11 female, 94% Caucasian) and 17 Never-Depressed Controls with no known first-degree relative with a psychiatric diagnosis ($M(SD)_{age}$= 24.5 ±6.4 , 11 female, 88% Caucasian) were recruited.
- Exclusions: significant eye problems, health problems, psychoactive drug or alcohol abuse within the past 6 months, history of psychosis, and manic episodes.

Neuroimaging

- fMRI data were collected with a 3.0-T Siemens Trio scanner. Functional volumes contained 32 oblique axial slices parallel to the AC/PC plane. Anatomical images were acquired using a standard T1-weighted spin-echo pulse sequence in the same space as the functional images using a finer in-plane resolution. Data was preprocessed using our standardized preprocessing stream.[12]

Autobiographical Problem-Solving Task

- Prior to scanning (~1hr) participants generated six of their most pressing unsolved problems and three words that captured the problem. E.g., My relationship with my family is very distant; Cue words: Family Distant Loss
- Participants were asked try to generate solutions to their problems while being scanned and to indicate if they were successful.

- **Subject Debriefing:**
  - Participants recounted their thoughts as they occurred during the APS task for each of their problems and rated the: (1) frequency with which they generally think of each problem, and (2) how sad and anxious they felt while thinking about each problem in the scanner.
  - Recounted thoughts were coded using a consensus approach to determine (1) problem severity, (2) stage of problem-solving achieved, (3) the degree of abstractness, and (4) solution effectiveness.

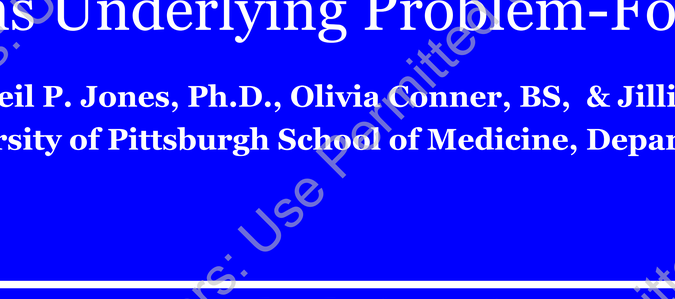
Methods (cont.)

Data Analysis

- The effect of APS was estimated according to the GLM. Single-subject data were modeled using a box-car function convolved with the canonical hemodynamic response function (HRF). The function contained appropriately placed models of the HRF for cue onset with fixation being modeled as the baseline, with the rating and inter-trial interval censored from analysis. A conjunction analysis was conducted to identify brain regions jointly correlated with experimenter-rated solution effectiveness and subject-rated successful solution generation. A t-test was used to examine group differences in the extracted ROI. A whole-brain analysis was conducted to examine group differences in APS related activity.

Results

Does the MDD group become stuck repetitively, and abstractly, thinking about their problems and emotions?



As shown in fig. 1, the MDD group reported engaging in more frequent, abstract, processing of more severe problems that were associated with more anxiety and sadness relative to controls. The MDD group also generated fewer and less effective solutions to their personal problems and became stuck during an earlier stage of problem-solving.

Does the MDD group demonstrate decreased activity in brain regions underlying effective solution generation?

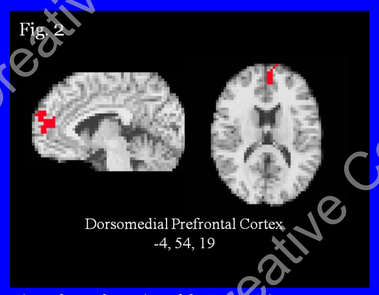
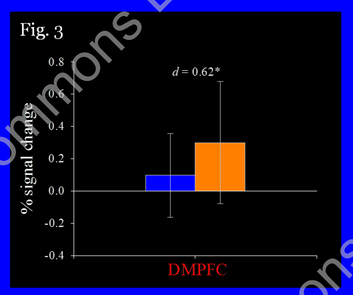


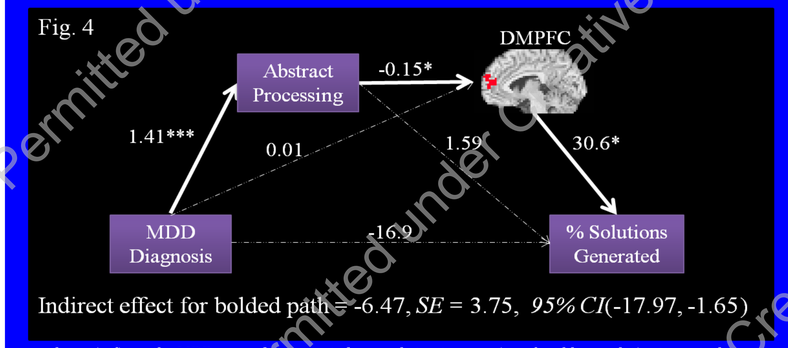
Fig. 2 shows the region of the DMPFC (p < .0025 uncorrected, p<.05 corrected) that was correlated with both subject-rated successful solution generation (r=.48, p=.005) and experimenter-rated solution effectiveness (r=.46, p=.007).



As shown in fig. 3, the MDD group demonstrated decreased activation in the DMPFC relative to the control group.

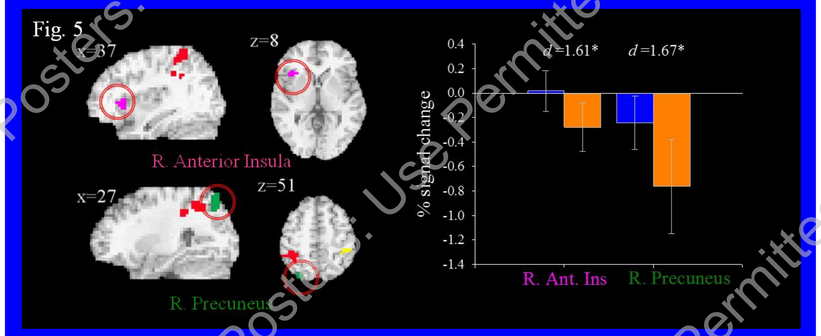
Results (cont.)

Are the observed deficits in solution generation in the MDD group relative to controls explained by increased abstract processing inhibiting DMPFC?



As shown in fig 4, the MDD group demonstrated more abstract processing of problems relative to controls, which was associated with decreased activation of DMPFC , which in turn was associated with a greater percentage of solutions generated .

Does the MDD group demonstrate increased activity in brain regions associated with greater elaboration of autobiographical information and increased emotion processing?



As shown in fig. 5, the MDD group demonstrated greater activation in the r. ant. ins. and r. precuneus relative to the control group (p< .005, uncorrected, p < .05 corrected). R. ant. ins. activation was correlated with both anxiety (r=0.39, p=0.027) and sadness (r = 0.44, p = 0.010). Within the MDD group precuneus activity was correlated with engagement in both instrumental rumination (r = 0.57, p =0.021)and emotion-focused rumination (r = 0.44, p =0.086)

Conclusions

- Individuals with MDD fail to generate effective solutions during APS because they do not engage the DMPFC to simulate potential outcomes of generated solutions. This failure appears to occur due to the abstractness of their thoughts which may serve to protect individuals with MDD by allowing them to avoid the more intense emotional experiences that arise when problems are directly faced.[12]

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