Supplementary Results

VHIS unilateral vmPFC and dlPFC lesions

Given the observed differences in depression severity between patients with bilateral vmPFC and dlPFC lesions, we conducted a follow-up analysis to determine whether unilateral vmPFC and dlPFC lesions would also have differential effects on depression. Among the VHIS participants, there were only three individuals with damage primarily affecting the vmPFC in only one hemisphere. This result can be explained by the lesion etiology. In every case the lesion resulted from a penetrating head injury (e.g. bullet or shrapnel). In cases where the penetration originated near the midline of the brain in the ventral PFC (e.g., slightly above and between the eyes), vmPFC in both hemispheres was typically damaged—a bilateral vmPFC lesion. In cases where the penetration originated more laterally, vmPFC damage could be confined to one hemisphere; however, in these cases ventrolateral PFC was typically damaged as well, often to a greater extent than vmPFC. The small number of focal, unilateral vmPFC lesions (two in the right hemisphere and one in the left hemisphere), precludes statistical analysis, however, we note that their BDI-II scores were relatively low (4, 11, and 2, respectively).

By contrast, there were a relatively large number of individuals with lesions mostly confined to dlPFC in one hemisphere (12 with right dlPFC lesions and 6 with left dlPFC lesions; Supplementary Fig. 2). In this unilateral dlPFC group (n=18), five individuals had BDI-II scores greater than 19 (indicating “high” levels of depression severity). Fisher’s exact test revealed that this proportion (5/18) was significantly greater than the non-PFC lesion group (10/101; p=.04), but not significantly different than the dorsal PFC

lesion group (3/5; p=.18). There was no evident laterality effect among the unilateral dlPFC lesions; of the five individuals with "high" levels of depression severity, two had left hemisphere lesions and three had right hemisphere lesions. The rating of depression severity for the unilateral dlPFC lesion group on the NRS was not significantly different from other groups, although the mean rating (1.50) was higher than the vmPFC lesion group (1.17), non-PFC lesion group (1.41), dorsal/ventral PFC lesion group (1.33), and non-brain-damaged group (1.37), but lower than the dorsal PFC lesion group (1.80).

Relationship between extent of ROI damage and BDI-II score

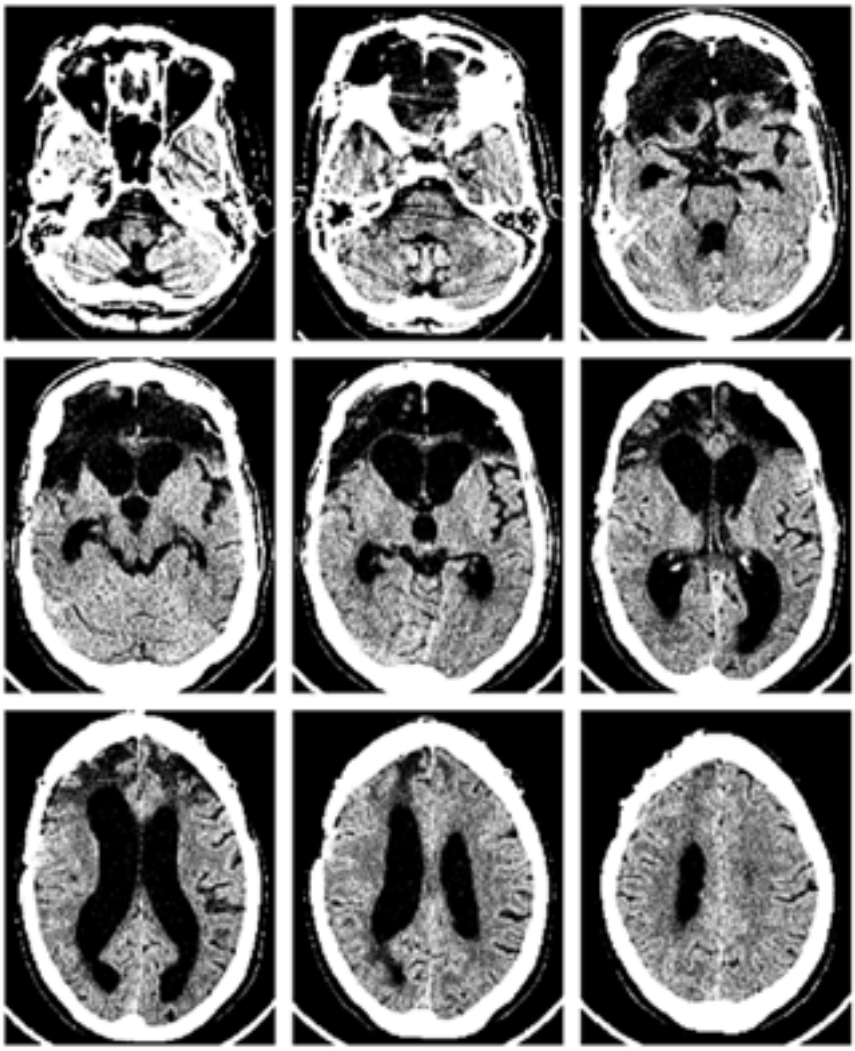
We investigated whether depression severity was related to the extent of damage to either vmPFC or dlPFC. Using data from all brain-injured VHIS veterans, we performed a multiple linear regression analysis with one dependent variable (BDI-II score) and two independent variables (percentage of damage to vmPFC and percentage of damage to dlPFC). The overall model approached significance ($F [2,193] = 2.6$, $p=.075$). The percentage of damage within vmPFC had a negative but nonsignificant relationship with BDI-II score ($t=-1.5$; $p=.12$), whereas the percentage of damage within dlPFC had a significant positive relationship with BDI-II score ($t=2.2$; $p=.03$), indicating that more extensive dlPFC damage was associated with higher overall BDI-II score.

Supplementary Table 1.

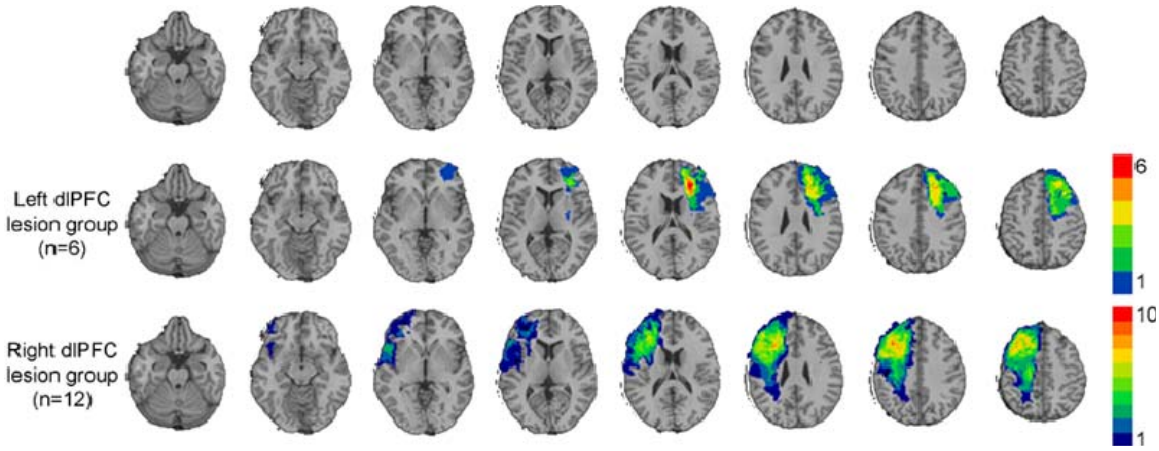
BDI symptom	Mean rating	Symptom Category
Sadness	.00	Cognitive/Affective
Punishment feelings	.00	Cognitive/Affective
Loss of interest	.00	Cognitive/Affective
Suicidal thoughts	.08	Cognitive/Affective
Self-dislike	.08	Cognitive/Affective
Indecisiveness	.15	Cognitive/Affective
Self-criticalness	.15	Cognitive/Affective
Guilty feelings	.15	Cognitive/Affective
Crying	.23	Cognitive/Affective
Irritability	.23	Cognitive/Affective
Past failure	.31	Cognitive/Affective
Loss of pleasure	.31	Cognitive/Affective
Changes in sleep	.31	Somatic
Loss of libido	.31	Neither
Change in appetite	.38	Somatic
Tiredness	.38	Somatic
Pessimism	.46	Neither

Mean severity scores for individual BDI items for the Iowa vmPFC patients. Scores are ordered from lowest mean severity rating (top) to highest mean severity rating (bottom). Only those items

that appear in both the BDI-IA and BDI-II are included. “Symptom Category” refers to the BDI-II factor analysis (Beck et al., 1996).



Supplementary Figure 1. CT image of patient following suicide attempt (axial slices). Ventral PFC is almost entirely destroyed, including vmPFC bilaterally (top row), whereas dorsal PFC is largely intact (bottom row).



Supplementary Figure 2. Unilateral dlPFC lesion overlaps. Color indicates the number of overlapping lesions at each voxel. Top row: Transverse slices of a normal healthy brain, for reference. From left to right, z=-22, -12, -2, 8, 18, 28, 38, and 48. In each slice the right hemisphere is on the reader's left (radiological convention). Second row: Lesion overlap for unilateral left dlPFC lesions. Third row: Lesion overlap for unilateral right dlPFC lesions.