Biology of Mood & Anxiety Disorders

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Michael T Treadway* and Diego A Pizzagalli*

Abstract

The neuroimaging literature of Major Depressive Disorder (MDD) has grown substantially over the last several decades, facilitating great advances in the identification of specific brain regions, neurotransmitter systems and networks associated with depressive illness. Despite this progress, fundamental questions remain about the pathophysiology and etiology of MDD. More importantly, this body of work has yet to directly influence clinical practice. It has long been a goal for the fields of clinical psychology and psychiatry to have a means of making objective diagnoses of mental disorders. Frustratingly little movement has been achieved on this front, however, and the 'gold-standard' of diagnostic validity and reliability remains expert consensus. In light of this challenge, the focus of the current review is to provide a critical summary of key findings from different neuroimaging approaches in MDD research, including structural, functional and neurochemical imaging studies. Following this summary, we discuss some of the current conceptual obstacles to better understanding the pathophysiology of depression, and conclude with recommendations for future neuroimaging research.

Keywords: Major Depression, Neuroimaging, PET, MRI, Serotonin, Dopamine, MRS, Glutamate, GABA, Inflammation

Introduction

M D D- (MDD) 250 P M . A MDD MDD D MDD

E . A . F M 1 . D MDD I j ( ) MDD. F

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Review

Neuroimaging and the pathophysiology of MDD

Morphometric neuroimaging studies

A MDD (ROI) 2,3 , (BM) 4 , 5 , 6 . MDD 3 . MDD, (ACC), (PFC), (OFC), (PFC), . A . F , 7,8 . I 9 . S . S 10,11 , 11-13 . I MDD. 14 MDD 15,16 , 17 . L MDD .

Functional neuroimaging studies

F MDD : (1) (2) (F 1). F : 18-20 .

Functional neuroimaging of emotion processing A . E 21-23 , 24,25 , 26-29 . F , PFC, (PFC), ACC, PFC. I . I 30,31 , .

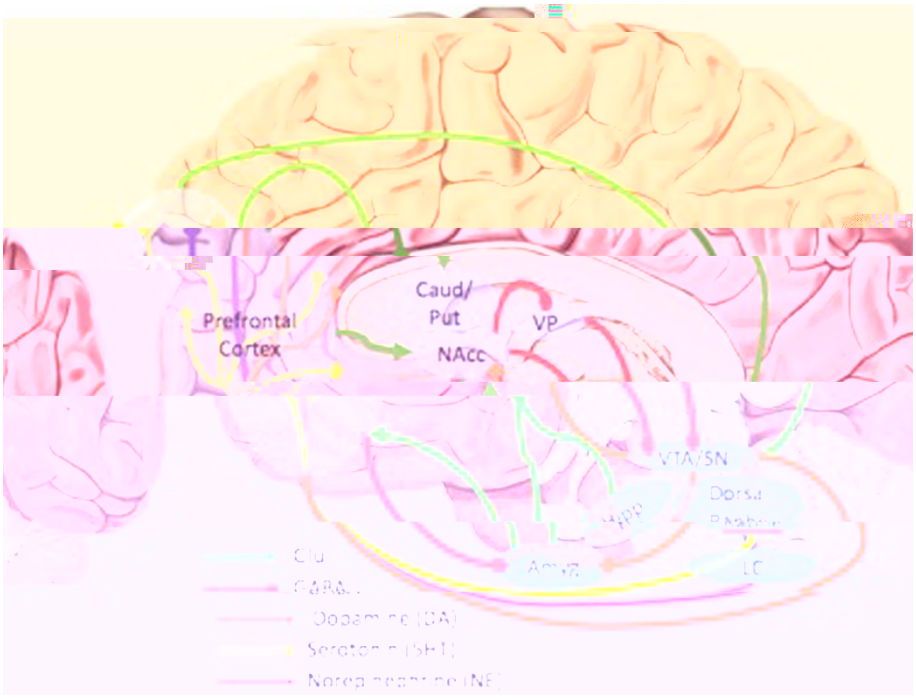

Figure 1 Regions, transmitters and circuits implicated in the pathology of major depressive disorder (MDD) by human neuroimaging studies. Past studies have identified alterations in monoamine levels and receptor availability as well as alterations in glutamate and GABA. These neurotransmitter systems participate in larger circuits involved in the experience and regulation of emotion, responses to stress, and processing of rewards. Note: placement of structure labels is approximate. Amyg = amygdala; Caud = Caudate; GABA = GABAergic projections; Glu = glutamatergic projections; Hipp = hippocampus; NAcc = nucleus accumbens; Put = Putamen; SN = substantia nigra; VP = ventral pallidum; VTA = ventral tegmental area. Republished with permission from Treadway and Zald [49].

32,33 . F MDD, I MDD . I PFC 34 . PFC 35 , . E . O 26 , 27-29 . MDD. C MDD

Functional neuroimaging of reward processing A - MDD (MRI) ( ) 36-38), 39-42 , 43,44 45-47 , 48 . I ,

Neurochemical imaging studies in MDD

Neurochemical imaging of serotonin systems in MDD

5-H

Neurochemical imaging of catecholamine systems in MDD O MDD (DA) (NE) 65,66 . DA 48,67,68 , 69,70 . 5-H , DA

N PE , SPEC MDD DA L-3,4 (L-DOPA) 71 , DA DA (DA). A 5-H DA . I PE SPEC DA , MDD 72 73-75 . I , DA SPEC , PE 76 SER DA (, β-CI) . M DA 77 . S DA MDD . I , D2/D3 78,79 . D2/D3 D2- 80 . O 81,82 , D2- (SSRI) 83 D1

(G) GABA, . A

G - GABA-

95

G GABA

MDD

G

96-98 .

G

(99). A MRS

MDD

G PFC/ACC 100 ,

G

. S

G PFC MDD

101-103 , 104

MDD 102 ,

MDD. H

MDD

G

(EC) 103 .

PE G

G

MDD 105 MDD 106 .

N- -D-

(NMDA) 107,108

G . F G

G PFC

95 . I

G MDD

G

MRI

G .

I G , GABA

MDD. GABA MDD

17,109 , GABA

110-112 ,

GABA PFC MRS

113,114 . M GABA

(HPA)-

115,116 . GABA

PFC,

GABA

GABA

Imaging neuroendocrine and neuroimmune systems in MDD

MRI. I

MDD,

( ),

(SH), 117,118 .

MDD ( ),

PFC 119,120 .

. A

121-124 . I

125 . G

60 ,

I

126,127 ,

128,129 . N

130,131 . A CNS 5-H DA 132,133 , 134,135 MDD PE 136 , B -O L D (BOLD) . O , M I D (MID) 137 , MDD 42 . F IFN-α . F v IFN-α DA PE DA ^{18}F D (F-DOPA) 50 . B MDD ( ), **Summary of neuroimaging studies** I , MDD . I MDD . N 20,138 (DBS) 139,140 (MS) 141 . B BOLD). M ROI ;) MDD, MDD . F , G GABA 143 . MDD (105,143). A 144,145 146,147 , ***Future directions and circuit-based analysis*** A MDD . I , . C . A , . B O

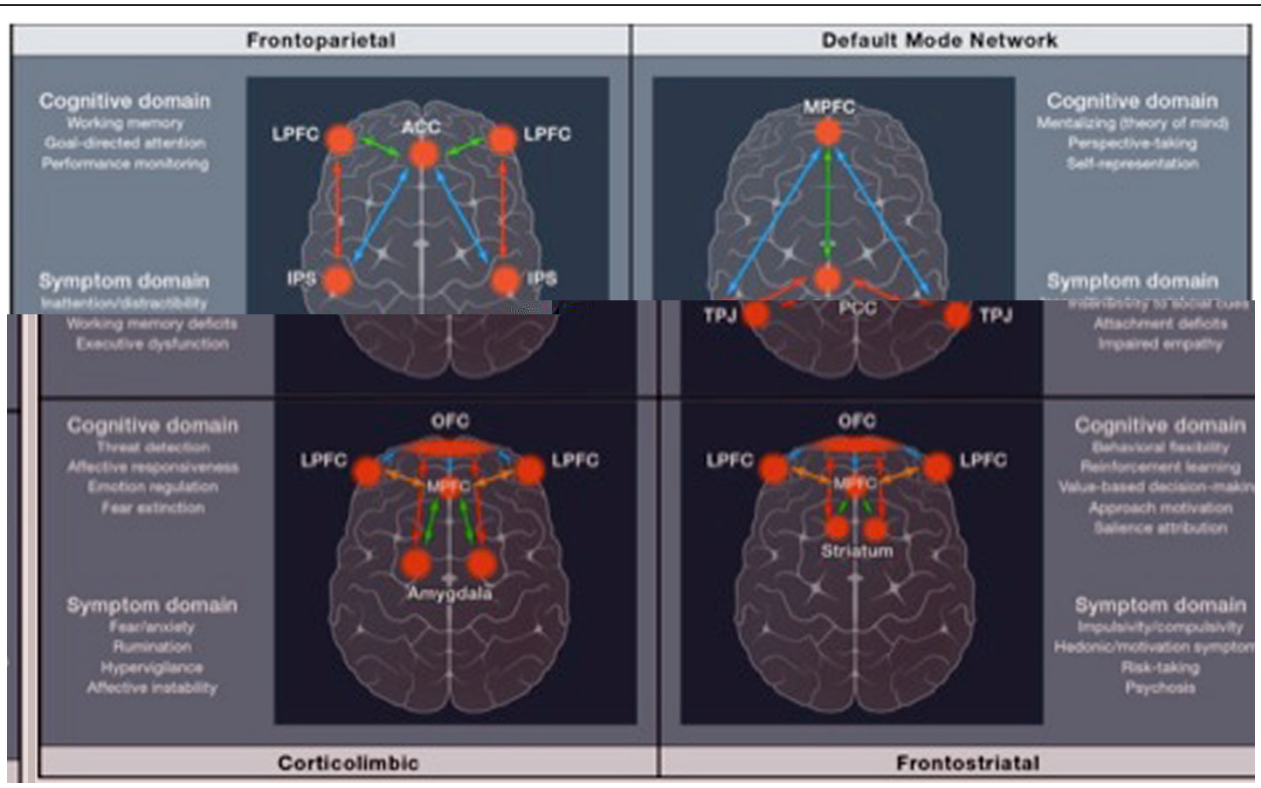

Figure 2 Schematic depiction of commonly identified functional networks and their associated cognitive and symptom domains.
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Conclusion

Abbreviations

5-HT: Serotonin; ACC: anterior cingulate cortex; BOLD: blood-oxygen level-dependent; CNS: central nervous system; DA: dopamine; DAT: dopamine transporter; DBS: deep-brain stimulation; dlPFC: dorsolateral prefrontal cortex; Glu: glutamate; GABA: gamma-aminobutyric acid; HPA axis: hypothalamic-pituitary-adrenal axis; IFN: interferon; MDD: major depressive disorder; MID: monetary incentive delay; mPFC: medial prefrontal cortex; MRI: magnetic resonance imaging; MRS: magnetic resonance spectroscopy; NE: norepinephrine; NET: norepinephrine transporter; OFC: orbitofrontal cortex; PET: positron emission tomography; PFC: prefrontal cortex; ROI: region of interest; SPECT: single photon emission computed tomography; SERT: serotonin transporter; TMS: transcranial magnetic stimulation; TSH: thyroid stimulating hormone; VBM: voxel-based morphometry; vlPFC: ventrolateral prefrontal cortex.

Competing interests
The authors declare no competing interests. Over the past three years, Dr. Pizzagalli received consulting/honoraria from AstraZeneca, Ono Pharma USA, Pfizer, Servier, and Shire for activities unrelated to the current review.

Authors' contributions
MTT and DAP developed the outline, MTT reviewed the relevant literature, and MTT and DAP wrote the manuscript. Both authors read and approved the final manuscript.

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