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Mechanisms Underlying Neurocognitive Dysfunctions in Recurrent Major Depression

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Recent work shows that depression is intimately associated with changes in cognitive functioning, including memory, attention, verbal □uency, and other aspects of higher-order cognitive processing. Changes in cognitive functioning are more likely to occur when depressive episodes are recurrent and to abate to some degree during periods of remission. However, with accumulating frequency and duration of depressive episodes, cognitive de□cits can become enduring, being evident even when mood improves. Such changes in cognitive functioning give depression links to mild cognitive impairment and thereby with neurodegenerative conditions, including Alzheimer's disease, Parkinson's disease, schizophrenia, and multiple sclerosis. Depression may then be conceptualized on a dimension of depression – mild cognitive impairment – dementia. The biological underpinnings of depression have substantial overlaps with those of neurodegenerative conditions, including reduced neurogenesis, increased apoptosis, reactive oxygen species, tryptophan catabolites, autoimmunity, and immune-in□ammatory processes, as well as decreased antioxidant defenses. These evolving changes over the course of depressive episodes drive the association of depression with neurodegenerative conditions. As such, the changes in cognitive functioning in depression have important consequences for the treatment of depression and in reconceptualizing the role of depression in wider neuroprogressive conditions. Here we review the data on changes in cognitive functioning in recurrent major depression and their association with other central conditions.

MeSH Keywords: Cognition • Depression • In□ammation • Neurogenesis • Oxidants

Abbreviations: ACTH – adrenocorticotropic hormone; AD – Alzheimer's disease; APOE – apolipoprotein E4; ASMT – N-Acetylserotonin O-methyltransferase; AVLT – auditory verbal learning test; AVP – arginine vasopressin; BDNF – brain-derived neurotrophic factor; CES-D – Center for Epidemiologic Studies Depression scale; CFS – chronic fatigue syndrome; CHC – chronic hepatitis C; CNS – central nervous system; COPD – chronic obstructive pulmonary disease; CRF – corticotrophin releasing factor; HDRS – Hamilton Depression Rating Scale; HIOMT – hydroxyindole-O-methyltransferase; HPA – hypothalamic-pituitary-adrenal axis; IDO – indoleamine 2,3-dioxygenase; IL – interleukin; LPS – bacterial lipopolysaccharide; MCI – mild cognitive impairment; MDA – malondialdehyde; MMSE – Mini-Mental State Examination; N-acetyl-5-methoxytryptamine – melatonin; NAS – N-acetylserotonin; NCAM – neural cell adhesion molecule; NCWd – Naming Color of Words Di□erent; NO – nitric oxide; OFC – orbitofrontal cortex; PD – Parkinson's disease; PFC –prefrontal cortex; rDD – recurrent depressive disorders; REM – rapid eye movement; ROS – reactive oxygen species; SLE – systemic lupus erythematosus; SSRIs – selective serotonin reuptake inhibitors; TAS – total antioxidant status; TDO – tryptophan 2,3-dioxygenase; TMT – Trail Making Test; TNF-α – tumor necrosis factor-alpha; TPGs – thiol protein groups; TrkB – tyrosine receptor kinase B; TRYCATs – tryptophan catabolites; VLPFC – ventrolateral prefrontal cortex

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6451 1 2 124

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