SMGroup

SM Journal of Depression Research and Treatment

Mini Review

First Line Antidepressant Medications: Brief Overview of Underlining Mechanisms

Fajemiroye O James*

Department of Pharmacological Sciences, Institute of Biological Sciences, Federal University of Goiás, Goiânia, Brazil

Article Information

Received date: Oct 27, 2016
Accepted date: Dec 18, 2016
Published date: Dec 22, 2016

***Corresponding author**

Fajemiroye O James, Department of Pharmacological Sciences, Institute of Biological Sciences, Federal University of Goiás, Goiânia, Brazil, Email: olulolo@yahoo.com

Article DOI 10.36876/smjdrt.1013

Abstract

Depression is a heterogeneous mental illness and one of the leading causes of disability worldwide. Poor understanding of neurobiology of depression and neural mechanisms of antidepressant drugs could be associated to their serendipitous discoveries. The first line of antidepressant medications (tricyclics, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, noradrenaline reuptake inhibitors, serotonin and noradrenaline reuptake inhibitors) are apparently ineffective in several patients. In principle, some of these antidepressant medications increase monoamine transmission directly (through serotoninergic or adrenergic receptors) or indirectly (by inhibiting the enzymatic breakdown and transport of serotonin and norepinephrine neurotransmitters). Meanwhile, other mechanistic hypotheses of antidepressant drugs have been linked to cholinergic transmission, γ-amino butyric acid, neuronal plasticity, hypothalamic pituitary adrenal axis, reward system, receptor activation or blockade (κ opioid receptor, cannabinoid receptor, cytokine-regulated pathways, Melatonin receptor), protein/enzyme inhibition (histone deacetylase, tissue plasminogen, vasopressin receptor, NK1 receptor antagonists, phosphor-diesterase inhibitors, circadian gene products. This review sought to highlight the neural structures, biomolecules and circuits that participate in the mechanisms of the first line antidepressant drugs. The contents of this review were retrieved from globally available database (Science Direct, PubMed, ACS, SciFinder, Scopus, Web of Science among others). Findings showed that, most of the first line antidepressant drugs are associated with different side effects and delayed therapeutic effects. The side effects are consequences of multiple interactions or mechanisms of antidepressant drug's action. The delayed effect otherwise called therapeutic action lag has been worsened by low level of adherence to long term antidepressant treatment. Researchers are still groping in the dark in their attempts to understand mechanisms of antidepressant drugs, promote development of fast acting drugs, improve medical diagnosis, drug prescription and ensure effective treatment of depression with little or no side effects of drugs.

Introduction

Depression is a serious debilitating psychiatric illness that constitute major problem for public health [1]. Despite the fact that depression is a mental illness that affects one-fifth of global population [2,3] number of mind boggling questions in respect of its pathogenesis [4] and unsatisfactory pharmacological intervention has kept researchers groping in the dark. Depression is considered as the fourth largest cause of disease's burden worldwide in 1990 and by 2020 it is expected to be the second [5]. Anedonia, low, sad or depressed mood are among the symptoms of depression [3]. The poor comprehension of the disease partly makes prescription of antidepressant drugs a daunting task. The cases of ever-increasing side effects including sexual dysfunction, dizziness, dysphoria, seizure, dry mouth nausea, vomiting, diarrhea, nervousness, insomnia, suicidal tendency, confusion etc. are disturbing. This review sought to highlight the neural structures, biomolecules and circuits that participate in the mechanisms of the first line antidepressant drugs. Methodological approach of this review include bibliographic search for scientific journals, books, and electronic media such as Science Direct, PubMed, etc. The search strategy for this review includes creation of search statements, usage of keywords or terms that are relevant to antidepressant drugs.

Neurobiology and Structural Circuits in Depressive State

The emergence of neuroimaging techniques such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), functional fMRI, lesion analysis studies among other technology have advanced means of clinical elucidation of the neurobiology of depression and understanding of the participating brain structures and biomolecules. Application of neuroimaging techniques have revealed morphological modifications of distinct neuroanatomical areas in depressed patients [6,7]. Magnetic resonance and PET studies show a reduction in the brain (frontal lobes, basal ganglia, amygdala, grey matter, hippocampus etc) volume of depressed patients and abnormalities in regional cerebral blood flow and glucose metabolism as well as alteration in cortical activities. These studies demonstrated hyper-activeness and enlargement of amygdala in depressed patients. These alterations explain higher susceptibility of patients with affective disorder to negative stimuli [8]. The use of resting-state functional connectivity magnetic resonance imaging (rs-fcMRI)

OPEN ACCESS

ISSN: 2573-3389

for the neural network function and dysfunction mapping [9] particularly abnormalities in the default-mode network and executive control network in depressed patients have detected alterations in intrinsic connectivity network [10].

The invaluable contributions of Paul Pierre Broca in 1878, James Papez in 1937, Yakovlev in 1948, Paul D. MacLean in 1952 have been phenomenal to the concept of limbic system and emotional behavior [11,14]. Up to date, it seems as if no consensus has been reached in respect of anatomical structures of the limbic system[15,16]. Meanwhile, limbic cortex (Cingulate gyrus, Parahippocampal gyrus), hippocampal formation (dentate gyrus, hippocampus, subicular complex), amygdala, septal area, hypothalamus among other anatomical components of limbic system are among brain structure being associated with emotion control[15,17]. The complexity of neural networks connecting these structures among others is of great challenges towards the understanding of the mechanism of emotional regulation. The association of the dysfunction within the anterior limbic network (which includes prefrontal regions) and sub cortical structures (such as the thalamus, striatum and the amygdala) to the spectrum of affective and cognitive symptomatology [18] is a typical example of challenges in understanding of the neurophysiology and neuropharmacology of this illness. The PFC, the amygdala and particularly the hippocampus are brain structures most widely studied in relation to depression. Prefrontal Cortex - PFC (involved in the planning of complex motor actions and conscious movement) is made of functional sections like ventromedial (VMPFC) and the dorsolateral (DLPFC) connected with each other via the cingulate gyrus and hippocampus [19]. The VMPFC is necessary for the normal generation of emotions and regulation of pain modulation, aggression, sexual and eating behaviors, autonomic and neuroendocrine responses [20]. In depressive state, failure of ventromedial and orbital prefrontal cortex control over amygdala could be associated with white matter lesions that disconnect PFC, the basal ganglia and the amygdala [8]. An impairment of Medial Prefrontal Cortex (MPFC) function could contribute to the neuroendocrine, autonomic, neurotransmitter, attention and reward-seeking abnormalities through that disinhibition of amygdala activity. The disinhibition of CRF release from the hypothalamic paraventricular nucleus by amygdala mediates the stressed component of glucocorticoid hormone secretion [21]. The fundamental role of hippocampus in learning and memory [22,23]as well as implication of alteration in hippocampal BDNF [24] made hippocampus one of the important brain structures that has been widely studied in depression. The Limbic-Cortical-Striatal-Pallidal-Thalamic Circuits (LCSPT), formed by connections between the Orbital And Medial Prefrontal Cortex (OMPFC), amygdala, hippocampal subiculum, ventromedial striatum, mediodorsal and midline thalamic nuclei and ventral pallidum [25] has been linked to emotional behaviour based on their anatomical connectivity with visceral control structures that mediate emotional expression, such as the hypothalamus and Periaqueductal Gray (PAG) [26]. The ventral tegmental area, nucleus accumbens, anterior cingulate (centre for integration of attentional and emotional output), paraventricular nucleus, raphe nucleus, nucleus basalis, locus ceruleus among other diencencephalic and brainstem nuclei play major roles in organizing the neuroendocrine, neurotransmitter, autonomic, and behavioural responses to stressors and emotional stimuli [27,28]. The mechanism of antidepressant actions of drugs is traceable to these structures and their associated biomolecules.

Some Neuronal Targets of Antidepressant Drugs

Some of the biomarker and susceptibility genes to affective disorders are traced to their role in neurotransmission, synthesis, transport, storage, metabolism, neural growth, differentiation, plasticity intracellular and extracellular signaling pathways among others. According to monoamine hypothesis of depression, monoamine (serotonin, noradrenaline and dopamine) dysfunction in the brain have been associated with depression [29,30]. Monoamine-based antidepressants remain the first line of therapy for depression despite their long therapeutic delays and low remission rates [31]. Monoamine Oxidase A (MAO-A) is considered a logical enzyme/biomolecule to investigate in depression because it regulates levels of major monoamines (serotonin, norepinephrine, and dopamine) in the brain [32]. Elevated MAO-A density was considered as the primary monoamine-lowering process during untreated major depression while monoamine transporter density was argued to play a secondary role towards long-term loss of specific monoamines [33]. The decrease in hippocampal volume among other brain region in some depressed patients supported a popular neurotrophic hypothesis of depression. Neurotrophic factors like Brain-Derived Neurotrophic Factor (BDNF) regulate neural growth and plasticity within adult brain [34,35]. Although preclinical studies have shown antidepressant effect of direct infusion of BDNF into the hippocampus [36] there are conflicting results that shows pro-depressant property of this protein in other brain region [37,38]. Hypercortisolaemia is also a feature of very severe depressive episodes [39]. This explains therapeutic efficacy of glucocorticoid antagonists [40]. Excessive release of glucocorticoids could elicits atrophic changes in hippocampal sub-regions [41]. Low level of glucocorticoids could attenuate its immunosuppressant effects and facilitate predominant of cytokines action as humoral mediators of innate or adaptive immunity. The action of cytokines in mood are widely documented [42,43]. Data in the literature suggest that inflammatory innate immune responses might contribute to the development of depression, in part through complex interactions with stress-responsive pathways involving the neuroendocrine and autonomic nervous systems. This pathway offers intriguing targets and therapeutic opportunities for depression [46].

Leading Classes of Antidepressant Drugs and their Mechanism of Action

Most of the report on CNS neurochemistry has shown vital role of noradrenaline, serotonin, dopamine, glutamatergic, gabaergic, cholinergic, endocanabinoid, peptidergic and hypothalamic-pituitary-adrenal pathways in depression. The use of wide variety of antidepressant drugs like ketamine, clorgyline, fluoxetine, imipramine, scopolamine [45,46] among others are evidences of the complexity of neural mechanisms. Few among the leading classes of antidepressant drugs are summarized as follows;

Selective Serotonin Reuptake Inhibitors (SSRIs):

SSRIs were developed as new generation of antidepressants in search for drugs with different mechanisms in an attempt to overcome some of the side effects that are associated with the traditional antidepressants. The assumption that selective agents would reduce side effects with increased "potency" spurred the development of SSRIs such as fluoxetine, paroxetine, sertraline, citalopram among others.

Noradrenaline reuptake inhibitors

These agents inhibit noradrenaline reuptake selectively. The first of such agent, reboxetine, has allowed clinical investigation of the role of the noradrenergic system in different aspects of depressive disorders. *In vitro* and *in vivo* pharmacological studies indicated that reboxetine has high affinity and selectivity for the human norepinephrine transporter over the serotonin and dopamine transporters [47].

Serotonin and noradrenaline reuptake inhibitors

The serotonin norepinephrine reuptake inhibitors like venlafaxine; a bicyclic phenylethylamine compound [48] and duloxetineare considered as dual action antidepressants that inhibit the reuptake of both serotonin (5-hydroxytryptamine) and norepinephrine [49]. In addition to the inhibition of both serotonin and noradrenaline at the presynaptic membrane, pharmacology of SNRIs also include weak affinity with receptors at the postsynaptic membrane, which expects well efficacy on major depressive disorder with less adverse effects in clinical use [50].

Tricyclics (TCAs)

The antidepressant action of TCAs has been associated to their inhibition of norepinephrine and serotonin reuptake in different proportions, down-regulation of postsynaptic receptors and subsequent changes in gene expression are ultimately responsible for the antidepressant action. Imipramine was the first TCA used in clinical practice following its unsuccessful trials as a potential antihistamine and antipsychotic [51,52]. Desipramine which is an antidepressant drug is the demethylated metabolite of imipramine. Clomipramine is one of the several tricyclic compounds approved for the treatment of depression by FDA.

Monoamine Oxidase Inhibitors (MAOI)

These are class of antidepressant drugs that inhibit activity of Monoamine Oxidase (MAO). MAO metabolizes and subsequently inactivate monoamine and indolamine neurotransmitters [53,54]. The antidepressant effects of MAO inhibition were discovered serendipitously when patients with tuberculosis were treated with iproniazid [55,56]. This event led scientists to hypothesize that a deficiency in norepinephrine, dopamine and possibly serotonin, may result in depression [57]. This hypothesis was substantiated by correlations between MAOI inhibition and mood improvement in depressed patients [58] and depletion studies of neurotransmitter precursors such as tryptophan and by the known mechanisms of antidepressant medications [59,61]. Tranylcypromine, moclobemide among others are widely utilized as antidepressant.

General Consideration

The development of the drugs in could be associated directly or indirectly with monoamine hypothesis. This hypothesis is vital to the aetiology of depression since the empirical discovery of the antidepressant property of monoamine oxidase inhibitors and tricyclics over fifty years ago [49]. Since then up to date, treatment of this disorder had witnessed high prescription of selective serotonin reuptake inhibitors (Fluoxetine, Citalopram), noradrenaline reuptake inhibitors (Atomoxetine, Reboxetine), serotonin and noradrenaline reuptake inhibitors (Duloxetine, Venlafaxine), monoamine oxidase inhibitors (Tranylcypromine, Phenelzine). However, cases of non-response to some of these monoamine - mechanism based drugs, series of avoidable side effects and seemingly opposing antidepressant mechanism of tianeptine - enhancement of serotonin reuptake [62] are incentives towards the discovery of newer or innovative agent with well defined and specific mechanism of action. In order to achieve the aim of getting a different and desirable response to antidepressant, there is need for a shift in research focus and orientation in respect of neuroanatomical, neurochemistry, neurobiology or genetic bases of depression. Development of non-pharmacological methods (e.g. deep brain stimulation, transcranial magnetic stimulation, and cognitive behavioral therapy) as well as combination of pharmacological and non-pharmacological procedures seems to be promising therapeutic approach for the treatment of depression [63].

Heterogeneity and comorbidity of depression with other disease could account for innumerous symptoms and sensitivity of patients to wider range of medication especially anxiolytic drugs. This disease symptomatological profile opens windows of opportunity for pharmacotherapy intervention. According to Berton & Nestler [29] potential non-monoamine neural target of antidepressant include κ opioid receptor antagonists, CB1 cannabinoid receptor agonists or antagonists, cytokine-regulated pathways, Melatonin receptor agonists, ligands at galanin's various receptors, NPY receptor agonists, histone deacetylase inhibitors, tissue plasminogen activator, CRF antagonists, vasopressin receptor antagonists, glucocorticoids agonists or antagonists, NK1 receptor antagonists, phosphodiesterase inhibitors, NMDA receptor antagonist, hypothalamic feeding peptides, circadian gene products, BDNF and other neurotrophic mechanisms. For instance, a modulation of glutamate neurotransmission or Kappa opioid receptor partial agonism could sufficiently induce antidepressant effect.

Conclusion and Future Perspective

There is no doubt that a comprehensive research can lead to new antidepressant drug discovery, for now, it is still a tall order to fully ascertain the exact biomarker of depression. Several preclinical models (in vitro, in vivo, ex vivo) such as acute or chronic stress, monoamine depletion, lesions, immune stimulation, exploration-based tests, social interaction-based tests, despair-based tests as well as quantification of proteins (neurotrophic factors, enzymes, transporter), measurement of enzyme activities (MAO, AChE) among others look promising in the search for the mechanism of antidepressant drugs. These models are designed in an attempt to satisfy face, predictive, constructive, aetiology and other validity. So far, cases of conflicting preclinical report and translation of experimental findings are troubling and require comprehensive studies among experts from different background.

There are still so much to be unraveled in respect to the neural mechanism of antidepressant drugs. The paradigm is now shifting from monoaminergic hypothesis of depression to other novel mechanisms. For instance, neuroinflammation seems to be a key pathological component of depression that involves neurotransmission, oxidative processes, neurotropic factors, neurotransmitter metabolism, and glucocorticoid functions in the central nervous system (CNS) and in the periphery [64]. Although, environment, genetics, existence of other diseases among others play important roles in human susceptibility to depression, efficacy and potency of antidepressant

drugs. Emerging cases or experiences of depressed patients still keep researchers groping in the dark. Limitations with the existing animal models, non-satisfactory level of success with current antidepressant, poor understanding of the endogenous and exogenous factors that predispose individual to depression remain great source of concern that demands collective efforts through interdisciplinary researches. Although preclinical research offer promising opportunities for new drug discovery, it needs to be accompanied by physiological stress response tests, measurement of different biomarkers (hormone levels, enzyme, signaling proteins, neurotrophic factors etc), recording of brain circuit dynamics in brain regions. In addition, researchers need to look beyond monoamine mechanisms.

References

1. Paykel ES. Depression: major problem for public health. Epidemiol Psichiatr Soc. 2006; 15: 4-10.
2. Manji HK, Drevets WC, Charney DS. The cellular neurobiology of depression. Nature Med. 2001; 7: 541-547.
3. Nestler EJ, Barrot M, DiLeone RJ, Eisch AJ, Gold SJ, Monteggia LM. Neurobiology of depression. Neuron. 2002; 34: 13-25.
4. Wayne CD, Joseph LP, Maura LF. Brain structural and functional abnormalities in mood disorders: implications for neurocircuitry models of depression. Brain Struct Funct. 2008; 213: 93-118.
5. Lopez AD, Murray CJ. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990-2020 and projected to 2020. Boston, MA. Harvard University Press. 1996.
6. Drevets WC. Neuroimaging studies of mood disorders. Biol Psychiatry. 2010; 48: 813-829.
7. Geuze E, Vermetten E, Bremner JD. MR-based in vivo hippocampal volumetrics: 2. Findings in neuropsychiatric disorders. Mol Psychiatry. 2005; 10: 160-184.
8. Nikola K, Abigail JS, Frank MS, Juliane M. Neurobiology of Depression and Novel Antidepressant Drug Targets. Curr Pharm Design. 2012; 18: 5791-5801.
9. Dosenbach NUF, Nardos B, Cohen AL, Fair DA, Power JD, Jessica AC, et al. Prediction of Individual Brain Maturity Using fMRI. Science. 2010; 329: 1358-1361.
10. Greicius MD, Flores BH, Menon V, Glover GH, Solvason HB, Kenna H, et al. Resting-state functional connectivity in major depression: Abnormally increased contributions from subgenual cingulate cortex and thalamus. Biol Psychiatry. 2007; 62: 429-437.
11. Nakano I. The limbic system: An outline and brief history of the concept. Neuropathology. 1998; 18: 211-214.
12. Papez JW. A proposed mechanism of emotion. Arch Neurol Psychiatry. 1937; 38: 725-743.
13. Yakovlev PI. Motility behavior and the brain: Stereodynamical organization and the neural coordinates of behavior. J Nerv Ment Dis. 1948; 107: 313-335.
14. Maclean PD. The triune brain in evolution. Role in paleocerebral functions. New York: Plenum Press. 1990.
15. Rajmohan V, Mohandas E. The limbic system. Indian Journal of Psychiatry. 2007; 49: 132-139.
16. Rolf K, Niels M. The limbic system: a review of its empirical foundation. Behav Brain Res. 1992; 52: 105-127.
17. Pierri JN, Lewis DA. Functional neuroanatomy. Sadock BJ, Sadock VA, editors. In: Kaplan and Sadock's Comprehensive textbook of psychiatry. 8th edn. Phildelphia: Lippincott William and Wilkins. 1, 3-33; 2005.
18. Strakowski SM, Del Bello MP, Adler CM. The functional neuroanatomy of bipolar disorder: A review of neuroimaging findings. Mol Psychiatry. 2005; 10: 105-116.
19. Palazidou E. The neurobiology of depression. British Medical Bulletin. 2012; 101: 127-145.
20. Ongur D, Price JL. The organization of networks within the orbital and medial prefrontal cortex of rats, monkeys and humans. Cereb Cortex . 2000; 10: 206-219.
21. Herman JP, Cullinan WE. Neurocircuitry of stress: central control of the hypothalamo-pituitary-adrenocortical axis. Trends Neurosci. 1997; 20: 78-84.
22. Squire LR, Knowlton BJ. The medial temporal lobe, the hippocampus, and the memory systems of the brain. M Gazzaniga, editor. In: The New Cognitive Neurosciences. 2nd Edn. Cambridge, MA: MIT Press. 2000; 765-779.
23. Howard E, Tim O, Cohen NJ. The Hippocampus What Does It Do? Behav Neural Biol. 1992; 57: 2-36.
24. Bun-Hee L, Yong-Ku K. The Roles of BDNF in the Pathophysiology of Major Depression and in Antidepressant Treatment. Psychiatry Investig. 2010; 7: 231-235.
25. Ongür D, Ferry AT, Price JL. Architectonic subdivision of the human orbital and medial prefrontal cortex. J Comp Neurol. 2003; 460: 425-449.
26. Nauta WJH, Domesick V. Afferent and efferent relationships of the basal ganglia. Ciba Found Symp. 1984; 107: 3-29.
27. Davis M, Shi C. The extended amygdala: are the central nucleus of the amygdala and the bed nucleus of the stria terminalis differentially involved in fear versus anxiety? Ann N Y Ac ad Sci. 1999; 877: 281-291.
28. Ledoux J. The emotional brain, fear, and the amygdala. Cell Mol Neurobiol. 2003; 23: 727-738.
29. Berton O, Nestler EJ. New approaches to antidepressant drug discovery: beyond monoamines. Natural Reviews Neuroscience. 2006; 7: 137-151.
30. Pittenger C, Duman RS. Stress, Depression, and Neuroplasticity: A convergence of mechanisms. Neuropsychopharmacology. 2008; 33; 88-109.
31. Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, et al. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. Am J Psychiatry. 2006; 163: 28-40.
32. Jeffrey HM, Nathalie G, Anahita B, Sandra S, Doug H, Armando G, et al. Elevated Monoamine Oxidase A Levels in the Brain. An Explanation for the Monoamine Imbalance of Major Depression. Arch Gen Psychiatry. 2006; 63: 1209-1216.
33. Shih JC, Chen K, Ridd MJ. Monoamine oxidase: from genes to behaviour. Annu Rev Neurosci. 1999; 22: 197-217.
34. Duman RS, Monteggia LM. A Neurotrophic model for stress-related mood disorders. Biol Psychiatry. 2006; 59: 1116-1127.
35. Monteggia LM, Barrot M, Powell CM, Berton O, Galanis V, Gemelli T, et al. Essential role of brain-derived neurotrophic factor in adult hippocampal function. Proc Natl Acad Sci USA. 2004; 101: 10827-10832.
36. Shirayama Y, Chen AC, Nakagawa S, Russell DS, Duman RS. Brain-derived neurotrophic factor produces antidepressant effects in behavioral models of depression. J Neurosci. 2002; 22: 3251-3261.
37. Krishnan V, Han MH, Graham DL, Berton O, Renthal W, Russo SJ, et al. Molecular adaptations underlying susceptibility and resistance to social defeat in brain reward regions. Cell. 2007; 131: 391-404.
38. Eisch AJ, Bolaños CA, de Wit J, Simonak RD, Pudiak CM, Barrot M, et al. Brain–derived neurotrophic factor in the ventral midbrain-nucleus accumbens pathway: a role in depression. Biol Psychiatry. 2003; 54: 994-1005.
39. Brouwer JP, Appelhof BC, Hoogendijk WJ, Huyser J, Endert E, Zuketto C, et al. Thyroid and adrenal axis in major depression: a controlled study in outpatients. Eur J Endocrinol. 2005; 152: 185-191.

Citation: Fajemiroye OJ. First Line Antidepressant Medications: Brief Overview of Underlining Mechanisms. SM J Depress Res Treat. 2016; 2(1): 1013. https://dx.doi.org/10.36876/smjdrt.1013

40. Schatzberg AF, Lindley S. Glucocorticoid antagonists in neuropsychotic disorders. Eur J Pharmacol. 2008; 583: 358-364.

41. McEwen BS. Physiology and neurobiology of stress and adaptation: central role of the brain. Physiol Rev. 2007; 87: 873-904.

42. Dunn AJ, Swiergiel AH, de Beaurepaire R. Cytokines as mediators of depression: what can we learn from animal studies? Neurosci Biobehav Rev. 2005; 29: 891-909.

43. Loftis JM, Hauser P. The phenomenology and treatment of interferon-induced depression. J Affect Disord. 2004; 82: 175-190.

44. Charles LR, Lucile C, Andrew HM. Cytokines sing the blues: inflammation and the pathogenesis of depression. Trends Immunol. 2006; 27: 24-31.

45. Furey ML, Drevets WC. Antidepressant efficacy of the antimuscarinic drug scopolamine: a randomized, placebo-controlled clinical trial. Arch Gen Psychiatry. 2006; 63: 1121-1129.

46. Hajos M, Fleishaker JC, Filipiak-Reisner JK, Brown MT, Wong EH. The selective norepinephrine reuptake inhibitor antidepressant reboxetine: pharmacological and clinical profile. CNS Drug Rev. 2004; 10: 23-44.

47. Thase ME, Sloan DME. Venlafaxine. Essentials of Clinical Psychopharmacology, Schatzberg AF, Nemeroff CB editors. In: American Psychiatric Publishing. Wahington DC. 2006; 159-170.

48. Dell'Osso B, Buoli M, Baldwin DS, Altamura AC. Serotonin norepinephrine reuptake inhibitors (SNRIs) in anxiety disorders: a comprehensive review of their clinical efficacy. Hum Psychopharmacol. 2010; 25: 17-29.

49. Schildkraut JJ. The catecholamine hypothesis of affective disorders: A review of supporting evidence. Am J Psychiatry. 1965; 122: 509-522.

50. Ipek KC, Oguz M, Guner U. Serotonin Noradrenaline Reuptake Inhibitors (SNRIs). Effects of Antidepressants. Dr. Ru-Band Lu. 2012.

51. Ban TA. Pharmacotherapy of depression: a historical analysis. J Neural Transm. 2001; 108: 707-716.

52. Kuhn R. The treatment of depressive states with G22355 (imipramine hydrochloride). Am J Psychiatry. 1958; 115: 459-464.

53. Amsterdam JD, Chopra M. Monoamine oxidase inhibitors revisited. Psychiatr Ann. 2001; 31: 361-370.

54. Livingston MG, Livingston HM. Monoamine oxidase inhibitors: An update on drug interactions. Drug Saf. 1996; 14: 219-227.

55. Crane GE. Iproniazid (Marsilid) phosphate, a therapeutic agent for mental disorders and debilitating diseases. Psychiatr Res Rep Am Psychiatr Assoc. 1957; 8: 142-152.

56. West ED, Dally PJ. Effects of iproniazid in depressive syndromes. Br Med J. 1959; 1: 1491-1494.

57. Schildkraut JJ. The catecholamines hypothesis of affective disorders: A review of current evidence. Am J Psychiatry. 1965; 122: 509-522.

58. Dunlop E, DeFelice EA, Bergen JR, Oscar R. The relationship between MAO inhibition and improvement of depression: Preliminary results with intravenous modaline sulfate (W3207B). Psychosomatics. 1965; 1-7.

59. Bymaster FP, McNamara RK, Tran PV. New approaches to developing antidepressants by enhancing monoaminergic neurotransmission. Expert Opin Investig Drugs. 2003; 12: 531-543.

60. Moreno FA, Heninger GR, McGahuey CA, Delgado PL. Tryptophan depletion and risk of depression relapse: A prospective study of tryptophan depletion as a potential predictor of depressive episodes. Biol Psychiatry. 2000; 48: 327-329.

61. Delgado PL, Charney DS, Price LH, Aghajanian GK, Landis H, Heninger GR. Serotonin function and the mechanism of antidepressant action: Reversal of antidepressant-induced remission by rapid depletion of plasma tryptophan. Arch Gen Psychiatry. 1990; 47: 411-418.

62. Kasper S, McEwen BS. Neurobiological and clinical effects of the antidepressant. CNS Drugs. 2008; 22: 15-26.

63. Dale E, Bang-Andersen B, Sánchez C. Emerging mechanisms and treatments or depression beyond SSRIs and SNRIs. Biochem. Pharmacol. 2015; 95: 81-97.

64. Sahin C, Dursun S, Cetin M, Aricioglu F. The neuroinflammation perspective of depression: Reuniting the outstanding mechanisms of the pathophysiology. Bulletin of Clinical Psychopharmacology. 2016; 26: 196-206.

Citation: Fajemiroye OJ. First Line Antidepressant Medications: Brief Overview of Underlining Mechanisms. SM J Depress Res Treat. 2016; 2(1): 1013. https://dx.doi.org/10.36876/smjdrt.1013