STM JOURNALS

Research & Reviews: A Journal of
Life Sciences

https://journals.stmjournals.com/rrjols/

ISSN: 2249–8656 (Online)
ISSN: 2348–9545 (Print)
Volume 15, Issue 1, 2025
DOI (Journal): 10.37591/RRJoLS

Research RRJoLS

# The Potential Role of Antidepressant Medications in DNA Oxidation of Depression Disorder Cases

Zainab Mahdi Jasim Al-Saygh*

***Abstract***

*Oxidative stress and DNA oxidation is a main target of different medications side effect, the current work aims to evaluate the potential role of anti-depressed medications in DNA oxidation in depression disorder cases, reactive oxygen species (ROS), total antioxidant (TAO) and 8-oxo deoxyguanine (8-oxo-dG) were detected in depressed disorder cases that treated with different medications included clomipramine, tryptizol, fluxetin, olanzapine, tryptizol with fluxetin, tryptizol with olanzapine and other types of medication. The results found significant differences in ROS and TAO (p 0.000), non-significant changes in 8-oxo-dG (p 0.649). In addition to non-sig in age (p 0.081) and sig changes in BMI (p 0.035) between cases and control groups. The ROS levels in subgroups showed significant changes (p 0.016), the cases treated with tryptizol and olanzapine have high level of ROS (160.34 ± 0.09), other types of medication have high level of ROS also (140 ± 7.96), then the cases tryptizol and fluxetin have (137.7 ± 53.35). The TAO have significant differences (p 0.000) among study subgroups clomipramine has high level of TAO (13.13 ± 2.0), tryptizol (10.3 ± 1.54), tryptizol with olanzapine have low level of TAO (8.21 ± 0.09) and other types have (8.13 ± 1.78), the 8-oxo-dG showed significant differences (p 0.01). The high level of 8-oxo-dG was observed in other medications (56.82 ± 3.92), then tryptizol with fluxetin (53.64 ± 0.09), low levels of oxidations were seen in clomipramine and olanzapine (14 ± 7.9, 14.6 ± 5.03). From the present outputs, we can conclude that clomipramine and olanzapine have antioxidant activity and a low effect in DNA oxidation.*

**Keywords:** Potential role, anti-depressed medications, DNA oxidation, ROS, TAO, depression disorder cases

## INTRODUCTION

Several pharmacological molecules with clinical impacts in depression disorder disease alter neurotransmission mediated by monoamines like serotonin [1], moreover, some biological effects of these molecules have been observed, like in bioenergetics, inflammation, and neurotrophic [2–4], the oxidative stress is An area that relates the excessive production of ROS through cellular respiration more than antioxidant capacity in the cellular system causing harmful effects in the cellular molecules like lipids, protein and nucleic acids [5, 6]. Nucleic acid oxidation is the basis of some diseases like cancer types and neurodegeneration [7, 8], mental disorders, and depression [9, 10].

***Author for Correspondence**
Zainab Mahdi Jasim Al-Saygh
E-mail: rababmahdi49@gmail.com

Assistant Lecturer, Department of Biology, Faculty of Education for Girls, University of Kufa, Iraq

Received Date: January 15, 2025
Accepted Date: January 17, 2025
Published Date: January 18, 2025

**Citation:** Zainab Mahdi Jasim Al-Saygh. The Potential Role of Antidepressant Medications in DNA Oxidation of Depression Disorder Cases. Research & Reviews: Journal of Life Sciences. 2025; 15(1): 41–47p.

The antidepressant drugs characterization influence on the level of DNA oxidation is documented by the connections between psychopathology (including affective disorders), aging, and mortality [11–13], evidence found that SSRIs may have antioxidant activity and lower lipid peroxidation in humans. Others suggested that this effect could be mediated by lowering the production of mitochondrial ROS [14–16], two intervention reports were enrolled in 45 and 22 cases have studied whether SSRIs treatment affects DNA damage by oxidation [17, 18]. Both studies

 

observed that SSRI therapy is related to decreased DNA oxidation using 8-oxo-7, 8-dihydro-2-deoxyguanosine (8-oxodG) as a marker. Another association between 8-oxodG and antidepressants was established in a pharmaco-epidemiological study [18], here, we test DNA damage by oxidative stress, in one hundred initially unmedicated patients with unipolar depression [19].

## METHODOLOGY

Study subjects: a cross-sectional study was implemented to detect the effect of different anti-depressed medications in the oxidative stress state. Samples were collected from cases were attended to privet psychiatric clinics suffered from depression disorder which was diagnosed by a specialist psychiatric physician. Written consent was obtained from each case before contributing to current study. The serum was isolated by a gel tube and transferred to the lab to detect ROS, 8-oxodG, and total antioxidant level. The cases used the following medications clomipramine, tryptizol, fluxetin, olanzapine, tryptizol with fluxetin, tryptizol with olanzapine, and other types of medication included (mirtazapine, lorazepam, tegretol and purelax) used in low percentage among patients in different dosages according to physician guide.

Data analysis: Data represented as mean ± SD, significant differences detected using independent sample t-test at p-value 0.05 and ANOVA one way (multiple comparisons).

## RESULTS AND DISCUSSION

The current work aims to the role of different anti-depressed drugs in the oxidative stress state rather than DNA oxidation in depressed disorder cases, the baseline characterization of study groups clarified in Table 1 significant differences in ROS and TAO (p0.000), non-significant changes in 8-oxo-dG (p 0.649). In addition to non-sig in age (p 0.081) and sig changes in BMI (p 0.035). The present output found the age of depression in individuals with moderate age, the age range of depressed patients in Iraq reported in young also in high percentage [20] found that pharmacy and medical students may be vulnerable to depression and anxiety. Another study found that the mean of age of depressed disorder was 29.8 years [21].

**Table 1.** Baselines characterization of study groups (depressed cases vs control group).

| Subjects | Case group | Control group | p |
|---|---|---|---|
| Age (year) | 39.50 ± 13.90 | 33.10±11.40 | 0.081 |
| BMI (kg/m$^2$) | 25.01 ± 3.86 | 28.06±5.41 | 0.035 |
| ROS (ηmol\l) | 110.5 ± 53.60 | 26.01±7.60 | 0.000 |
| TAO (ηmol\l) | 11.80 ± 2.30 | 19.00±4.36 | 0.000 |
| 8-oxo-dGηg/ml | 29.40 ± 19.66 | 26.50±22.10 | 0.649 |

The oxidative stress represented in the present work by ROS and TAO levels, the ROS was significantly elevated in depressed cases and this result was proved in previous studies implemented [22, 23]. The same results were reported in a study of unipolar depression that found the lowered concentration of antioxidants and higher concentrations of malondialdehyde implicate the high level of oxidative stress. The long exposure period of psychological stress is a vital factor for major depression, elevation in levels of malondialdehyde, oxidative stress, and depressive symptoms [24]. Other evidence found that the biomarkers of oxidative stress like superoxide dismutase, malondialdehyde, and nitrite are altered in depressive disorders [25, 26].

The DNA oxidation represented by 8-oxo-dG that referred to DNA damage by ROS effect, the oxidative DNA damage was significantly correlated with the severity of depressive symptoms in a Cohort study [27]. Slightly elevation in 8-oxo-dG in depressed cases than the control group [28, 29] reported that the oxidative damage is a potent genotoxic factor that stimulates DNA damage response that has functional implications to cellular function, that maintains the integrity and function of DNA

 

or lead to cell apoptosis orinduce cellular senescence when the absence of response to DNA damage [30].

The cases used the following medications that patients classified into subgroups according to it; clomipramine, tryptizol, fluxetin, olanzapine, tryptizol with fluxetin, tryptizol with olanzapine and other types of medication used in low percentage among patients. The ROS levels in subgroups showed significant changes among subgroups (p 0.016), the cases treated with tryptizol and olanzapinehave high levels of ROS (160.34 ± 0.09), other types of medication have high levels of ROS also (140 ± 7.96), then the cases tryptizol and fluxetin have (137.7 ± 53.35) (Figure 1).

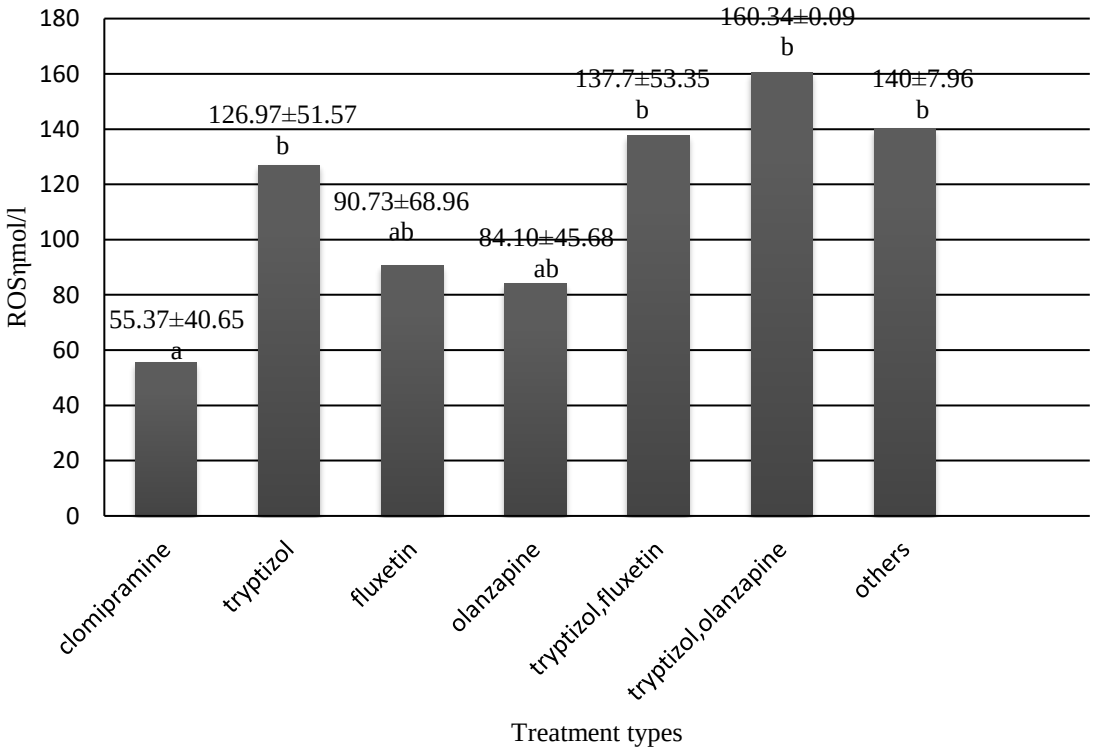


**Figure 1.** The ROS level in study subgroups included treatment types (significant differences p 0.016, ANOVA one-way, different letters referred to significant among groups).

The TAO has significant differences (p 0.000) among study subgroups clomipramine has a high level of TAO (13.13 ± 2.0), tryptizol (10.3 ± 1.54), tryptizol with olanzapine have a low level of TAO (8.21 ± 0.09) and other types have (8.13 ± 1.78) (Figure 2).

DNA oxidation was detected in the present research by test 8-oxo-dG, the results that showed significant differences (p 0.01). The high level of 8-oxo-dG was observed in other medications (56.82±3.92), then tryptizol with fluxetin (53.64 ± 0.09), low levels of oxidations were seen in clomipramine and olanzapine (14 ± 7.9, 14.6 ± 5.03) (Figure 3).

The treatment subgroup causes decreased in ROS and elevated TAO in some types of antidepressants medications would be correlated with a decrease in damage of systemic nucleic acid by oxidation of a sample of patients with depression disorder. There was the largest clinical study investigating the impacts of antidepressant therapy on systemic DNA damage level by oxidation, a highly significant lowered in the DNA and the RNA oxidation marker after treatment was observed, and the level of urinary 8-oxodG is higher in severe psychiatric disorders cases in compared with healthy peoples [31–33] this agree with our output.

 

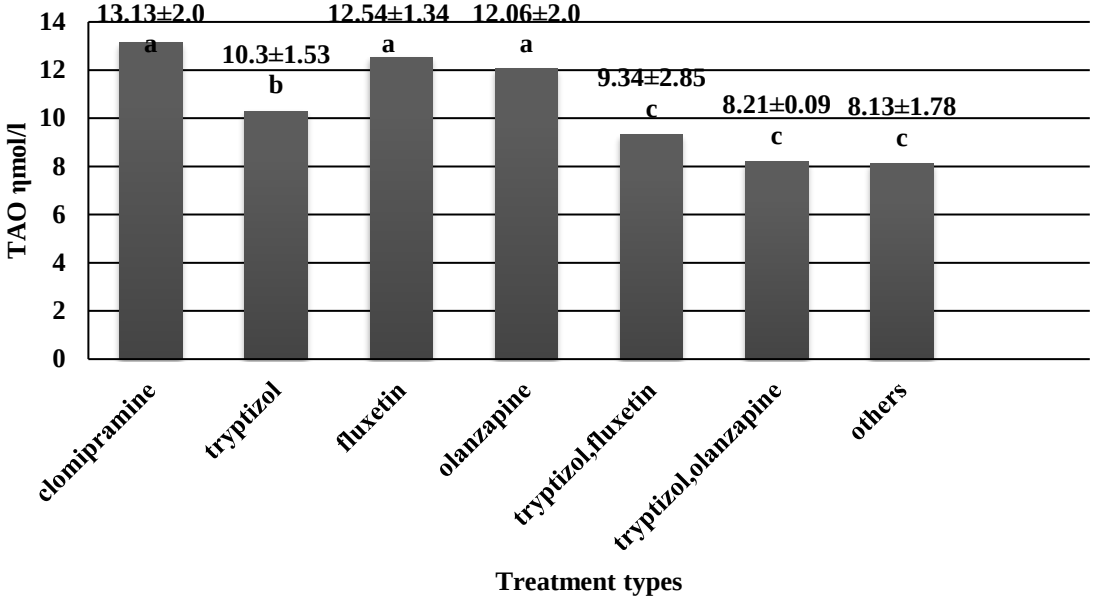


**Figure 2.** The TAO level in study subgroups included treatment types (significant differences p 0.000, ANOVA one-way, different letters referred to significant among groups).

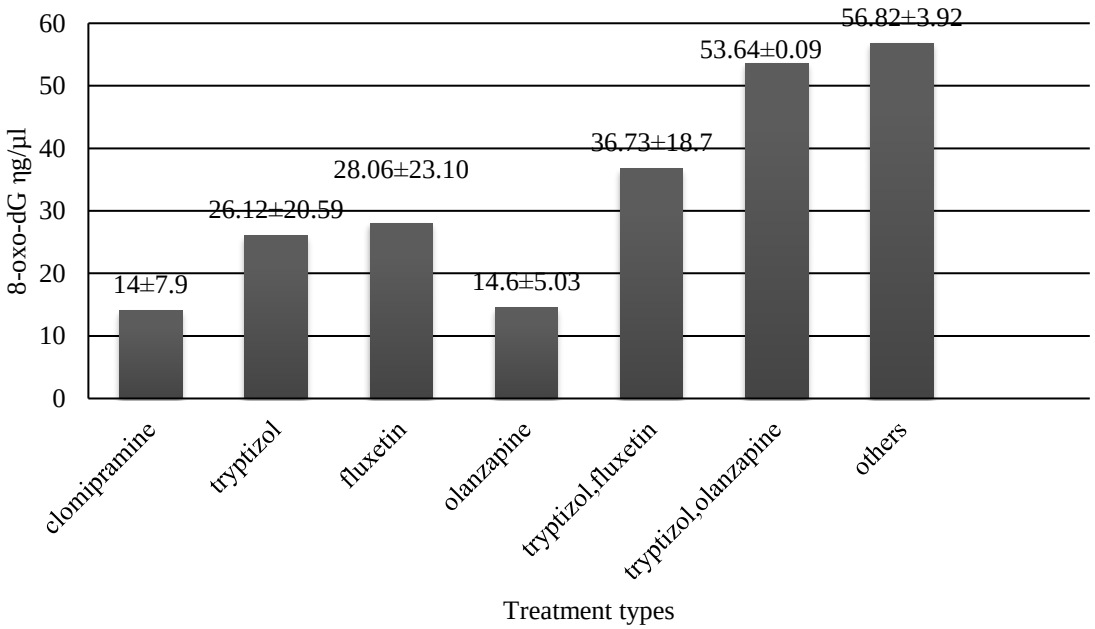


**Figure 3.** The 8-oxo-dG level in study subgroups included treatment types (significant differences p 0.01, ANOVA one-way, different letters referred to significant among groups).

The mechanisms of antidepressant drugs underlie a reduction of nucleic acid oxidation [34] and clarified that in cortical neurons, serotonin stimulates mitochondrial respiration, and increases antioxidant enzymes expression as well as catalase and superoxide dismutase 2 and decreased ROS production. These events were mediated by receptor (5-$HT_{2A}$) and subsequent modulator activation of the mitochondrial pathway, the SIRT1-PCG-1α axis. The ROS reduction and enhancing antioxidant mechanism would eliminate the oxidative modifications of nucleic acids and other cell components against oxidative stress. The 5-$HT_{2A}$ receptor and serotonin transporter are distributed in other sites like platelets and the liver [35], belong to this fact [36] supposed that a plausible the CNS and/or peripheral

 

blockade of the serotonin transporter caused by an SSRI, that lead to elevation in extracellular 5-HT level, could cause decreased intracellular oxidative stress by mitochondrial function altering by activation of 5-$HT_{2A}$.

The origin of 8-oxodG in the fluids are not known to yet, studies suggest that is released from enzymatic repair of DNA and/or the nucleotide pool, the repair or degraded capacity of oxidized nucleotides more than were formed it thus their levels in fluids, the level of oxidized nucleotide in urine is thought to not depend on the rate of repair/degradation but on the rate of formation [37].

The present work agrees with other evidence that found a strong association of DNA oxidation and oxidative stress with depression and medication therapy [38–40].

There were some limitations in the present study including the small size of samples because of restricted awareness about the mental health and psychiatric therapy among peoples [41–43], in addition to the unrecorded high number of depression cases in the Iraqi population, thus further studies should be created to enhance information about medications and its effect in DNA [44, 45].

## CONCLUSIONS

From the current work, we can conclude that the oxidative stress represented by ROS and TAO had a strong association with depressed patients, non-significant elevation in DNA oxidation was observed in depression patients, the medication types have a significant effect in the ROS, TAO, and 8-oxo-dG in significant differences, the clomipramine and olanzapine have antioxidant activity and low effect in DNA oxidation.

## REFERENCES

1. Cipriani A, Zhou X, Del Giovane C, Hetrick SE, Qin B, Whittington C, Coghill D, Zhang Y, Hazell P, Leucht S, Cuijpers P. Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis. Lancet. 201627;388(10047):881–890.
2. Wang L, Wang R, Liu L, Qiao D, Baldwin DS, Hou R. Effects of SSRIs on peripheral inflammatory markers in patients with major depressive disorder: a systematic review and meta-analysis. Brain Behav Immun. 2019;79:24–38.
3. Østergaard L, Jørgensen MB, Knudsen GM. Low on energy? An energy supply-demand perspective on stress and depression. Neurosci Biobehav Rev. 2018;94:248–270.
4. Kraus C, Castrén E, Kasper S, Lanzenberger R. Serotonin and neuroplasticity–links between molecular, functional and structural pathophysiology in depression. Neurosci Biobehav Rev. 2017;77:317–326.
5. Pilar-Cuéllar F, Vidal R, Díaz A, Castro E, dos Anjos S, Pascual-Brazo J, Linge R, Vargas V, Blanco H, Martínez-Villayandre B, Pazos Á. Neural plasticity and proliferation in the generation of antidepressant effects: hippocampal implication. Neural Plast. 2013;2013(1):537265.
6. Fakouri NB, Hou Y, Demarest TG, Christiansen LS, Okur MN, Mohanty JG, Croteau DL, Bohr VA. Toward understanding genomic instability, mitochondrial dysfunction and aging. FEBS J. 2019;286(6):1058–1073.
7. Schumacher B, Pothof J, Vijg J, Hoeijmakers JH. The central role of DNA damage in the ageing process. Nature. 2021;592(7856):695–703.
8. Nunomura A, Lee HG, Zhu X, Perry G. Consequences of RNA oxidation on protein synthesis rate and fidelity: implications for the pathophysiology of neuropsychiatric disorders. Biochem Soc Trans. 2017;45(5):1053–1066.
9. Castellani RJ, Nunomura A, Rolston RK, Moreira PI, Takeda A, Perry G, Smith MA. Sublethal RNA oxidation as a mechanism for neurodegenerative disease. Int J Mol Sci. 2008;9(5):789–806.
10. Blackburn EH, Greider CW, Szostak JW. Telomeres and telomerase: the path from maize, Tetrahymena and yeast to human cancer and aging. Nat Med. 2006;12(10):1133–1138.

 

11. Pousa PA, Souza RM, Melo PH, Correa BH, Mendonça TS, Simões-e-Silva AC, Miranda DM. Telomere shortening and psychiatric disorders: a systematic review. Cells. 2021;10(6):1423.
12. Leone M, Kuja-Halkola R, Leval A, D'Onofrio BM, Larsson H, Lichtenstein P, Bergen SE. Association of youth depression with subsequent somatic diseases and premature death. JAMA Psychiatry. 2021;78(3):302–310.
13. Archer G, Kuh D, Hotopf M, Stafford M, Richards M. Association between lifetime affective symptoms and premature mortality. JAMA Psychiatry. 2020;77(8):806–813.
14. Copeland WE, Keen R, Tong G, Shanahan L. Negative life events and emotional symptoms from ages 2 to 30 years. JAMA Network Open. 2024;7(8):e2429448.
15. Jimenez-Fernandez S, Gurpegui M, Diaz-Atienza F, Pérez-Costillas L, Gerstenberg M, Correll CU. Oxidative stress and antioxidant parameters in patients with major depressive disorder compared to healthy controls before and after antidepressant treatment: results from a meta-analysis. J Clin Psychiatry. 2015;76(12):13705.
16. Cumurcu BE, Ozyurt H, Etikan I, Demir S, Karlidag R. Total antioxidant capacity and total oxidant status in patients with major depression: impact of antidepressant treatment. Psychiatry Clin Neurosci. 2009;63(5):639–645.
17. Gerö D, Szoleczky P, Suzuki K, Módis K, Oláh G, Coletta C, Szabo C. Cell-based screening identifies paroxetine as an inhibitor of diabetic endothelial dysfunction. Diabetes. 2013;62(3):953–964.
18. Lopez-Vilchez I, Diaz-Ricart M, Navarro V, Torramade S, Zamorano-Leon J, Lopez-Farre A, Galan AM, Gasto C, Escolar G. Endothelial damage in major depression patients is modulated by SSRI treatment, as demonstrated by circulating biomarkers and an in vitro cell model. Transl Psychiatry. 2016;6(9):e886.
19. Tutakhail A, Nazari QA, Khabil S, Gardier A, Coudore F. Muscular and mitochondrial effects of long-term fluoxetine treatment in mice, combined with physical endurance exercise on treadmill. Life Sci. 2019;232:116508.
20. Palta P, Samuel LJ, Miller III ER, Szanton SL. Depression and oxidative stress: results from a meta-analysis of observational studies. Psychosomat Med. 2014;76(1):12–19.
21. Ahmadimanesh M, Abbaszadegan MR, Morshedi Rad D, Moallem SA, Mohammadpour AH, Ghahremani MH, Farid Hosseini F, Behdani F, Akhondpour Manteghi A, Jowsey P, Shabani Behbahani F. Effects of selective serotonin reuptake inhibitors on DNA damage in patients with depression. J Psychopharmacol. 2019;33(11):1364–1376.
22. Black CN, Bot M, Scheffer PG, Penninx BW. Oxidative stress in major depressive and anxiety disorders, and the association with antidepressant use; results from a large adult cohort. Psychol Med. 2017;47(5):936–948.
23. Köhler-Forsberg K, Jorgensen A, Dam VH, Stenbæk DS, Fisher PM, Ip CT, Ganz M, Poulsen HE, Giraldi A, Ozenne B, Jørgensen MB. Predicting treatment outcome in major depressive disorder using serotonin 4 receptor PET brain imaging, functional MRI, cognitive-, EEG-based, and peripheral biomarkers: a neuropharm open label clinical trial protocol. Front Psychiatry. 2020;11:641.
24. Kathem SH, Al-Jumail AA, Noor-Aldeen M, Najah N, Ali Khalid D. Measuring depression and anxiety prevalence among Iraqi healthcare college students using hospital anxiety and depression scale. Pharm Pract (Granada). 2021;19(2).
25. Tripathi R, Alqahtani SS, Meraya AM, Makeen HA, Tripathi P, Pancholi SS. Evaluation of depression, anxiety, and stress among university healthcare students. J Appl Pharm Sci. 2022;12(10):78–87.
26. Al-Hamzawi AO, Bruffaerts R, Bromet EJ, AlKhafaji AM, Kessler RC. The epidemiology of major depressive episode in the Iraqi general population. PloS One. 2015;10(7):e0131937.
27. Jawad MA, Al-Terehi MN, Enad HA, Kareem TJ, Lazim AI. Estimation the oxidative stress state in depression disorders patients. Clin Schizophr Relat Psychoses. 2021;15.
28. Al-Terehi MN, Kadhim AJ, Mohsen IH, Alsaffar MF, Atiyah S, Hasan SY, Hamad DA, Bustani GS, Abdullah SA, Ramadhan RS. Association of 8-Oxo-2'-Deoxyguanosine, hOGG1 Ser326Cys gene polymorphism with reactive oxygen species in depression patients. Clin Schizophr Relat Psychoses. 2021;15.

 

29. Tsuboi H, Tatsumi A, Yamamoto K, Kobayashi F, Shimoi K, Kinae N. Possible connections among job stress, depressive symptoms, lipid modulation and antioxidants. J Affective Disord. 2006;91(1):63–70.
30. Ozcan ME, Gulec M, Ozerol E, Polat R, Akyol O. Antioxidant enzyme activities and oxidative stress in affective disorders. Int Clin Psychopharmacol. 2004;19(2):89–95.
31. Del Rio D, Stewart AJ, Pellegrini N. A review of recent studies on malondialdehyde as toxic molecule and biological marker of oxidative stress. Nutr Metab Cardiovasc Dis. 2005;15(4):316–328.
32. Vieira EL, Mendes-Silva AP, Ferreira JD, Bertola L, Barroso L, Vieira M, Teixeira AL, Diniz BS. Oxidative DNA damage is increased in older adults with a major depressive episode: A preliminary study. J Affective Disord. 2021;279:106–110.
33. Jackson SP, Bartek J. The DNA-damage response in human biology and disease. Nature. 2009;461(7267):1071–1078.
34. Bernardini L, Barbosa E, Charão MF, Goethel G, Muller D, Bau C, Steffens NA, Santos Stein C, Moresco RN, Garcia SC, Souza Vencato M. Oxidative damage, inflammation, genotoxic effect, and global DNA methylation caused by inhalation of formaldehyde and the purpose of melatonin. Toxicol Res. 2020;9(6):778–789.
35. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. Hallmarks of aging: An expanding universe. Cell. 2023;186(2):243–278.
36. Jorgensen A, Krogh J, Miskowiak K, Bolwig TG, Kessing LV, Fink-Jensen A, Nordentoft M, Henriksen T, Weimann A, Poulsen HE, Jorgensen MB. Systemic oxidatively generated DNA/RNA damage in clinical depression: associations to symptom severity and response to electroconvulsive therapy. J Affective Disord. 2013;149(1-3):355–362.
37. Jorgensen A, Köhler-Forsberg K, Henriksen T, Weimann A, Brandslund I, Ellervik C, Poulsen HE, Knudsen GM, Frokjaer VG, Jorgensen MB. Systemic DNA and RNA damage from oxidation after serotonergic treatment of unipolar depression. Transl Psychiatry. 2022;12(1):204.
38. Munkholm K, Poulsen HE, Kessing LV, Vinberg M. Elevated levels of urinary markers of oxidatively generated DNA and RNA damage in bipolar disorder. Bipolar Disord. 2015;17(3):257–268.
39. Fanibunda SE, Deb S, Maniyadath B, Tiwari P, Ghai U, Gupta S, Figueiredo D, Weisstaub N, Gingrich JA, Vaidya AD, Kolthur-Seetharam U. Serotonin regulates mitochondrial biogenesis and function in rodent cortical neurons via the 5-HT2A receptor and SIRT1–PGC-1α axis. Proc Natl Acad Sci U.S.A. 2019;116(22):11028–11037.
40. Ruddell RG, Mann DA, Ramm GA. The function of serotonin within the liver. J Hepatol. 2008;48(4):666–675.
41. Jorgensen A, Broedbaek K, Fink-Jensen A, Knorr U, Soendergaard MG, Henriksen T, Weimann A, Jepsen P, Lykkesfeldt J, Poulsen HE, Jorgensen MB. Increased systemic oxidatively generated DNA and RNA damage in schizophrenia. Psychiatry Res. 2013;209(3):417–423.
42. Poulsen HE, Nadal LL, Broedbaek K, Nielsen PE, Weimann A. Detection and interpretation of 8-oxodG and 8-oxoGua in urine, plasma and cerebrospinal fluid. Biochim Biophys Acta Gen Subj. 2014;1840(2):801–818.
43. Jorgensen A, Krogh J, Miskowiak K, Bolwig TG, Kessing LV, Fink-Jensen A, Nordentoft M, Henriksen T, Weimann A, Poulsen HE, Jorgensen MB. Systemic oxidatively generated DNA/RNA damage in clinical depression: associations to symptom severity and response to electroconvulsive therapy. J Affective Disord. 2013;149(1–3):355–362.
44. Villa RF, Ferrari F, Gorini A, Brunello N, Tascedda F. Effect of desipramine and fluoxetine on energy metabolism of cerebral mitochondria. Neurosci. 2016;330:326–334.
45. Herbet M, Szumełda I, Piątkowska-Chmiel I, Gawrońska-Grzywacz M, Dudka J. Beneficial effects of combined administration of fluoxetine and mitochondria-targeted antioxidant at in behavioural and molecular studies in mice model of depression. Behav Brain Res. 2021;405:113185.

 