The Causes, Prevention and Treatment of Adolescent Depression: A Review

Jiacheng Li, Shenyu Zhou, Meifan Zhu

1 Syracuse University, NY, United States
2 The Stony Brook School, NY, United States
3 Tomas Jefferson School, MO, United States

ABSTRACT
Depression is an increasingly common phenomenon among adolescents, and it is a serious mental health problem for adolescents. The objective of this study was to systematically review the causes, prevention, and treatment of adolescent depression. The next part reviewed potential causes of adolescent depression. This part of the review focused on on predicting causes of adolescent depression from family factors, stressful negative life events, genetic vulnerability, and gender differences. Last, clinical aspects of adolescent depression are reviewed, including treatments and prevention of depression in adolescence. In short, effective treatments and prevention have been found already in treating adolescent depression. Adolescents suffering from depression become more common with different causes. Still, as long as clinicians use early intervention in adolescents with depression, the long-term burden of disease could be reduced.

Keywords: adolescent depression, factors, disorders, treatment

1. INTRODUCTION
Adolescence, or childhood, depression is by definition a type of depressive mood disorder shown by feeling sad and the loss of interest in activities. That is similar to adult major depressive disorder, especially when different symptoms teenagers may suffer from increased irritability and behavioral dyscontrol instead of sadness and hopelessness [1]. Adolescence with stress, experiencing a major loss, facing social, developmental challenges, or other mental disorders (e.g., anxiety disorder, conduct disorder, behavioral disorder, etc.) are more susceptible to depression. Adolescent depression could involve high levels of anxiety and, in severe cases, suicidal intent [2]. Meanwhile, according to Eapen and Crnec, approximately 8% of children and adolescents suffer from adolescent depression [3].

The characteristics and diagnostic criteria of depression are similar and correspond to each other. The symptoms of depression can be used as a diagnostic criterion for depression. In Depression: A cognitive perspective, Beck used internal mental representations to show that depression can affect a person's cognition, it means depression would affect the mood of the sufferer, so the characteristics of depressed people were found to be a sense of loss, failure, and worthlessness, and the sufferer would have negative emotions and opinions about everything [4]. Also, according to the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), people with depression may experience low mood, decreased interest in all activities, slower thinking, and fatigue. These symptoms must last for two weeks or more to be diagnosed as depression [5].

MDD (Major depressive disorders) in adolescence are common compared to other disorders within their age group. For incidence, the number of MDD patients, notably in girls, increases sharply after puberty, and by the end of adolescence, a one-year prevalence rate...
The burden is highest in low-income and middle-income countries [6, 7].

Since MDD is strongly associated with the substantial present, morbidity in the future, and the rising suicide risks [7-9]. This problem has become traumatic also to society. They give adolescents great fear and concern in their aging process, as well-reviewed psychological and physical risk factors.

Two examples - psychologically - could be on family histories and exposure to psychosocial stress [10]. Other side effects can include developmental factors, sex hormones, and psychosocial adversity interacts to increase risk through hormonal factors and many cases, perturbed neural pathways [9-11]. So, adolescent treatment, which includes antidepressants, is doubtful, and some opinions about clinical management differ among individuals [7,8]. In this case, prevention strategies targeted at high-risk groups are exceptionally promising [8]. Therefore, this current research will be devoted to a social solution for preventing the disorder and pared with the most effective psychological interference/therapy - including a discussion and data prove for the ineffectiveness of antidepressants. In this passage first, an overview of some potential causes of adolescent depression will be presented. Next, some treatments that may help adolescent depression patients will be concluded.

2. CAUSES

2.1. Family factors

Parental depression and family psychiatric history have been confirmed to correlate with children’s risk of developing major depressions [1]. Family history of depression would also affect adolescents’ risk of depression. While the correlation is not as high and as clear as it is for children, biological or hormonal factors and social stresses would have a greater contribution to the development of depression for adolescents [12]. The effects and impacts of family psychiatric history may span over three generations, from grandparents to the most recent generation [13]. Goodman and Gotlib in 1999 proposed four mechanisms that would explain the transmission of the risk of depression between mother and adolescents, 1) heritability of depression; 2) innate neuroregulatory dysfunction; 3) exposure to negative maternal cognitions, behaviors, and affects, and 4) the stressful living environment of the children [14]. Although most literature emphasized the effects mothers had on their children, paternal factors are equally critical. From the research conducted by Sanford et al. in 1995, low positive involvement between the father and the child and more conflicts with the fathers would induce more severe adolescent depression. Meanwhile, this research suggests that paternal and maternal variables contributed separately to the condition of adolescent depression [15].

Family emotional climate is another causing factor for child depression. The disruption and alternation in traditional social and family structures, alone with family relationships of affectionless control, low cohesion, and high discord, would be important predictors of child pathology involving child depression [16]. Parental depression is a powerful predictive factor for child mental disorders of depression and anxiety. While affectionless control is strongly suggestive and predictive for youth depression with non-depressed parents, family discord and low cohesion would be vital for other child pathology predictions, yet not for child depression [17]. Besides, past study suggests that negative family interaction, including low family support and family conflict, contributes to the development of youth depression; and they are also predictors of youth depression [18].

2.2. Daily Stress and Stressful Negative Life Events

Depression increases when adolescents experience challenges as they grow up. At this stage of understanding, we could argue that when teenagers’ life pressures are higher, the risk of depression will increase. Stress is a big factor that leads to depression. In the daily life of teenagers, the pressure comes from studying. Rodrigo et al.’s research shows that many young students have symptoms of anxiety and depression, and induced causes of these symptoms are mainly caused by study pressure [19]. Meanwhile, it is important to note that self-esteem is an important psychological factor for adolescents. In the growth of adolescents, adolescents often have fragile self-esteem. Self-esteem is closely related to research on adolescents. From this standpoint, self-esteem also plays an important role in social development [20]. There is also a relationship between self-esteem and depression in adolescence, and many studies have confirmed [21].

Studying pressure is only one factor of adolescent depression. Sokratus et al. suggested that minor events in life can also influence depression in adolescence, such as dropping out of school, family financial difficulties, losing friends, and so on [22]. Not only that, but sudden major events in life can also impact mental health for adolescents. The reason is that sudden negative events also create psychological and physical stress for adolescents [23]. Hankin also said, “almost all individuals with a depressive disorder will have encountered at least one significant negative life event in the month before the onset of depression” [24]. Thus, Reinerherz et al. found that such negative life events as loss of a loved family, parental divorce, and suicide are all factors that can lead to depression in
adolescents [25]. These stressful negative events can build up and eventually lead to depression. But using the data of researches on stressful life events and adolescent depression, Birmaher et al. found that it is difficult to establish a causal relationship between negative life events and depression [26]. This is exactly with the findings of Hankin, who indicated that stress and depression are bidirectional and that they can both be a cause or a consequence [24].

2.3. Gender and depression

Compared with the environmental effects and biological age maskers, differences between gender have also been studied and questioned by socialists and psychologists. Gender depression varied significantly due to aging factors.

Before puberty, the possibility of boys developing MDD is greater than girls. However, a colossal conversion happens when their reach puberty/adolescence. There were twice as many females developing MDD during their adolescent years compared [9,13]. Another data set shows the lifetime risk of depressive patients in the United States, 21% in females and 13% in males [14]. Depressed females typically experience recurrent depression more than depressed males, including side effects such as greater weight gain, anxiety, and physical manifestations of their depressive disorders [9].

The reason for such an outstanding difference could be explained by scientific factors that are special on females or males during their puberty/adolescence. One factor is the scientific chemical - monoamine tryptophan depleton, which is important in decreasing serotonin transmission [27, 28]. Also, the PET (positron emission tomography) demonstrated decreased serotonin synthesis in females compared with males after tryptophan was depleted [29]. Elevated levels of serotonin, and the serotonin metabolite 5-HIAA, were found only in women [28]. This could be strongly tied with a larger availability of the serotonin transporter in females [30]. Different factors/suggestions of the data gap between two genders consist of both cultural and biological factors.

3. TREATMENT

3.1. Interpersonal psychotherapy

Interpersonal psychotherapy (IPT) is an evidence-based, time-limited, specifically focused method in treating mood disorders [31]. Interpersonal psychotherapy for adolescents (IPT-A) was adapted from IPT, as strong evidence suggests its benefits for treating adult mood disorder, including bipolar disorder and major depressive disorder [32, 33]. IPT-A is a time-limited and effective individual psychotherapy treatment for adolescents with a mood disorder, including depressive disorder and major depression [34]. IPT-A, as well as IPT, aims at the goals of 1) alleviate depressive symptoms; 2) enhance social communication and decrease stress in relationships; 3) increase awareness of the mood symptoms and their effects on interpersonal events [35]. Specific problem areas (s) will be identified and focused on during the treatment (Grief, Role Transition, Role Dispute, Interpersonal Deficits). An Independent study indicates the effectiveness of IPT-A. The randomly assigned depressed youngsters receiving IPT-A demonstrated noticeable improvement in social functioning, compared with youth who received ordinary treatment [36]. Other studies also signify the usefulness of IPT-A in preadolescent depression [37].

Therapy typically involves 12 sessions, once per week, with each session lasting approximately 45 to 60 minutes. The sessions would be divided into 1) initial phase (sessions 1-4); 2) middle phase (sessions 5-9); 3) termination phase (sessions 10-12) [35]. In the initial phase, the IPT-A psychiatrist would generally perform diagnosis, psychoeducation, and explain treatment. In the middle phase, the therapist would keep work with the adolescent in the identified problem area and help the teen with communication skills and problem-solving strategies. In the termination phase, the therapist would discuss with the teen about the experience and progress of the treatment; and the therapist would comment with the patient and the patient’s family whether further sessions are needed [35]. IPT-A could be conducted in hospitals, school-based clinics, community psychological clinics, or private clinics; professionals with a master's degree in clinical or counseling psychology or in social work who received IPT-A training.

3.2. Antidepressants

Because depressive illnesses during this period are associated with negative long-term consequences, including suicide, additional psychiatric comorbidity, interpersonal relationship problems, it’s exceptionally important to find a suitable treatment. There is no clear cut evidence to support the concerns of the marked suicidal aspect on the effects accruing in depressed adolescents being treated with SSRIs [38-40]. It shows how clinical benefits we judge and outweigh the risks of neurodevelopment and are an important therapeutic choice in treating moderate to severe adolescent depression [41]. However, in this section, bringing up a comparison between the most widely used antidepressants and placebos would give suggestions to a wider range of patients.

In recent years a worldwide controversy has begun discussing the efficacy of antidepressants on adolescents developing depression. It specifically hinges on meta-
analyses that mostly propose which antidepressants are either effective or not on the scale compared with placebo. According to a study done by [42], it suggested the tolerability of antidepressants is poorly characterized in adolescents with depressive and anxiety disorders [43]. Among adverse events that affect the tolerability of antidepressants in youth is activation. Symptoms may include impulsivity, restlessness, and/or insomnia [44]. These symptoms have the side effect of serotonin and mostly serotonin norepinephrine inhibitors (SSRIs and SSNRIs) back in the 1990s. Nevertheless, until now, activations such as prevalence, risk factors, and pathophysiology are still poorly recognized [45].

### 3.3. Behavioral Activation

Behavioral Activation is considered psychotherapy for the treatment of depression. Behavioral activation has also been used for a long time as a treatment for depression. Behavioral activation started the development through Lewinsohn's exploration of pleasant events scheduling [46.47]. And BA was later used by Beck et al. and constituted a cognitive therapy [48]. Now, according to a study by Dimidjian et al., BA has been shown to be as effective as antidepressants in patients with depression [49]. BA is a solution-centered intervention, and BA is a simple therapy [50]. Through the analysis of Lorie A. Ritschel et al., because patients with depression tend to be avoidant, they get fewer opportunities for extrinsic rewards [51]. The main role of BA happens to be to modify the environmental factors that lead to patients' depressive symptoms [52].

BA is defined as structured psychotherapy. There are three aims, increasing more positive activities that make patients have feelings of pleasure, decreasing more negative activities that make patients have bad ideas, solving limitation of reward. Because depression is characterized by behavioral avoidance, the three aims of BA can be customized according to the patient's situation [53]. To achieve these aims, therapists and patients work together to create a system of tasks, task assignments, and activities that increases the chances of positive rewards and reduces the chances of avoidance [54]. Because each patient's needs are different, the therapist adjusts tasks and activities accordingly. Instead of increasing the amount of activity, the therapist discusses with the patient what types of activities are beneficial for the patient [55]. And because there is a trend in psychology and psychiatry to adopt more individualized approaches to more effective treatment options for patients [55, 56]. So, BA can be an effective treatment for adolescent depression.

### 4. CONCLUSION

This study reviews the causes, prevention, and treatment of adolescent depression.

Depression has a significant negative impact of any aspect on adolescents, particularly with a long-term burden of disease. There are many potential factors for depression in adolescents, but many effective treatments have been studied and proven to intervene and prevent patients. It is important to note that the earlier starting intervention and treatment, the less harmful the depression will be to adolescence.

### REFERENCES

[1] Birmaher, B., Ryan, N. D., Williamson, D. E., Brent, D. A., Kaufman, J., Dahl, R. E., ... & Nelson, B. (1996). Childhood and adolescent depression: a review of the past 10 years. Part I, Journal of the American Academy of Child & Adolescent Psychiatry, 35(11), 1427-1439. doi:10.1097/00004583-199611000-0001

[2] Eapen, V., & Črnčec, R. (2012). Strategies and challenges in the management of adolescent depression. Current Opinion in Psychiatry, 25(1), 7-13. doi:10.1097/yco.0b013e32834de3bd

[3] Shaffer D, Gould MS, Fisher P, et al. Psychiatric Diagnosis in Child and Adolescent Suicide. Arch Gen Psychiatry. 1996;53(4):339 - 348. doi:10.1001/archpsyc.1996.01830040075012

[4] Beck, A. T. (1967). Depression: Clinical, experimental, and theoretical aspects. New York: Hoeber Medical Division.

[5] American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (DSM-5), Fifth edition.

[6] Birmaher, B., Brent, D. A., Kolko, D., Baughner, M., Bridge, J., Holder, D., Iyengar, S., & Ulloa, R. E. (2000). Clinical outcome after short-term psychotherapy for adolescents with major depressive disorder. Archives of general psychiatry, 57(1), 29 - 36. https://doi.org/10.1001/archpsyc.57.1.29

[7] Harrington, R., Whittaker, J., Shoebridge, P., & Campbell, F. (1998). Systematic review of efficacy of cognitive behaviour therapies in childhood and adolescent depressive disorder. BMJ (Clinical research ed.), 316(7144), 1559 - 1563. https://doi.org/10.1136/bmj.316.7144.1559

[8] Lewinsohn, P. M., Rohde, P., & Seeley, J. R. (1998). Major depressive disorder in older adolescents: prevalence, risk factors, and clinical implications. Clinical psychology review, 18(7), 765 - 794. https://doi.org/10.1016/s0272-7358(98)00010-5
[9] Cyranowski, J. M., Frank, E., Young, E., & Shear, M. K. (2000). Adolescent onset of the gender difference in lifetime rates of major depression: a theoretical model. Archives of general psychiatry, 57(1), 21 - 27. https://doi.org/10.1001/archpsyc.57.1.21

[10] Denmeade, S. R., & Isaacs, J. T. (2010). Bipolar androgen therapy: the rationale for rapid cycling of supraphysiologic androgen/ablation in men with castration resistant prostate cancer. The Prostate, 70(14), 1600 - 1607. https://doi.org/10.1002/pro.21196

[11] Li, C. E., DiGiuseppe, R., & Froh, J. (2006). The roles of sex, gender, and coping in adolescent depression. Adolescence, 41(163), 409 - 415.

[12] Albert P. R. (2015). Why is depression more prevalent in women?. Journal of psychiatry & neuroscience : JPN, 40(4), 219 - 221. https://doi.org/10.1503/jpn.150205

[13] Sander, J. B., & McCarty, C. A. (2005). Youth depression in the family context: familial risk factors and models of treatment. Clinical child and family psychology review, 8(3), 203 - 219. https://doi.org/10.1007/s10567-005-6666-3

[14] Goodman, S. H., & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: a developmental model for understanding mechanisms of transmission. Psychological review, 106(3), 458 - 490. https://doi.org/10.1037/0033-295x.106.3.458

[15] Sanford, M., Szatmari, P., Spinner, M., Munroe-Blum, H., Jamieson, E., Walsh, C., & Jones, D. (1995). Predicting the one-year course of adolescent major depression. Journal of the American Academy of Child and Adolescent Psychiatry, 34(12), 1618 - 1628. https://doi.org/10.1097/00004583-199512000-00012

[16] Weissman, M. M., & Jensen, P. (2002). What research suggests for depressed women with children. The Journal of clinical psychiatry, 63(7), 641 - 647. https://doi.org/10.4088/jcp.v63n0717

[17] Nomura, Y., Wickramaratne, P. J., Warner, V., Mufson, L., & Weissman, M. M. (2002). Family discord, parental depression, and psychopathology in offspring: ten-year follow-up. Journal of the American Academy of Child and Adolescent Psychiatry, 41(4), 402 - 409. https://doi.org/10.1097/00004583-200204000-00012

[18] Sagrestano, L. M., Paikoff, R. L., Holmbeck, G. N., & Fendrich, M. (2003). A longitudinal examination of familial risk factors for depression among inner-city African American adolescents. Journal of family psychology : JFP : journal of the Division of Family Psychology of the American Psychological Association (Division 43), 17(1), 108 - 120.

[19] Rodrigo, C., Welgama, S., Gurusinghe, J. et al. (2010). Symptoms of anxiety and depression in adolescent students; a perspective from Sri Lanka. Child Adolesc Psychiatry Ment Health 4, 10. https://doi.org/10.1186/1753-2000-4-10

[20] Steinberg, L., & Morris, A. S. (2001). Adolescent development. Annual review of psychology, 52(1), 83-110.

[21] Sowislo, J. F., & Orth, U. (2013). Does low self-esteem predict depression and anxiety? A meta-analysis of longitudinal studies. Psychological bulletin, 139(1), 213.

[22] Sokratous, S., Merkouris, A., Middleton, N., & Karanikola, M. (2013). The association between stressful life events and depressive symptoms among Cypriot university students: a cross-sectional descriptive correlational study. BMC public health, 13(1), 1-16.

[23] Compas, B. E., Howell, D. C., Phares, V., Williams, R. A., & Ledoux, N. (1989). Parent and child stress and symptoms: An integrative analysis. Developmental Psychology, 25(4), 550.

[24] Hankin, B. L. (2006). Adolescent depression: Description, causes, and interventions. Epilepsy & behavior, 8(1), 102-114.

[25] Reinherz, H. Z., Giaconia, R. M., Pakiz, B., Silverman, A. B., Frost, A. K., & Lefkowitz, E. S. (1993). Psychosocial risks for major depression in late adolescence: A longitudinal community study. Journal of the American Academy of Child & Adolescent Psychiatry, 32(6), 1155-1163.

[26] Birmaher, B., Ryan, N. D., Williamson, D. E., Brent, D. A., Kaufman, J., Dahl, R. E., ... & Nelson, B. (1996). Childhood and adolescent depression: a review of the past 10 years. Part I. Journal of the American Academy of Child & Adolescent Psychiatry, 35(11), 1427-1439.

[27] Salk, R. H., Hyde, J. S., & Abramson, L. Y. (2017). Gender differences in depression in representative national samples: Meta-analyses of diagnoses and symptoms. Psychological bulletin, 143(8), 783 - 822. https://doi.org/10.1037/bul0000102

[28] Xiao, L., & Becker, J. B. (1994). Quantitative microdialysis determination of extracellular striatal...
dopamine concentration in male and female rats: effects of estrous cycle and gonadectomy. Neuroscience letters, 180(2), 155-158.

[29] Weissman, M. M., Bland, R., Joyce, P. R., Newman, S., Wells, J. E., & Wittchen, H. U. (1993). Sex differences in rates of depression: cross-national perspectives. Journal of affective disorders, 29(2-3), 77-84.

[30] Kessler, R. C., McGonagle, K. A., Zhao, S., Nelson, C. B., Hughes, M., Eshleman, S., ... & Kendler, K. S. (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Archives of general psychiatry, 51(1), 8-19.

[31] Markowitz, J. C., & Weissman, M. M. (2004). Interpersonal psychotherapy: principles and applications. World psychiatry: official journal of the World Psychiatric Association (WPA), 3(3), 136 - 139.

[32] Frank, E., Kupfer, D. J., Thase, M. E., Mallinger, A. G., Swartz, H. A., Fagiolini, A. M., Grochocinski, V., Houck, P., Scott, J., Thompson, W., & Monk, T. (2005). Two-year outcomes for interpersonal and social rhythm therapy in individuals with bipolar I disorder. Archives of general psychiatry, 62(9), 996 - 1004. https://doi.org/10.1001/archpsyc.62.9.996

[33] Frank, E., Kupfer, D. J., Wagner, E. F., McEachran, A. B., & Cornes, C. (1991). Efficacy of interpersonal psychotherapy as a maintenance treatment of recurrent depression. Contributing factors. Archives of general psychiatry, 48(12), 1053 - 1059. https://doi.org/10.1001/archpsyc.1991.01810360017002

[34] Mufson, L., & Sills, R. (2006). Interpersonal Psychotherapy for depressed adolescents (IPT-A): an overview. Nordic journal of psychiatry, 60(6), 431 - 437. https://doi.org/10.1080/08039480601022397

[35] Miller, L., Hlastala, S. A., Mufson, L., Leibenluft, E., & Riddle, M. (2016). Interpersonal Psychotherapy for Adolescents With Mood and Behavior Dysregulation: [36] Evidence-Based Case Study. Evidence-based practice in child and adolescent mental health, 1(4), 159 - 175. https://doi.org/10.1080/23794925.2016.1247679

[36] Mufson, L., Dorta, K. P., Wickramaratne, P., Nomura, Y., Olsson, M., & Weissman, M. M. (2004). A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents. Archives of general psychiatry, 61(6), 577 - 584. https://doi.org/10.1001/archpsyc.61.6.577

[37] Dietz, L. J., Weinberg, R. J., Brent, D. A., & Mufson, L. (2015). Family-based interpersonal psychotherapy for depressed preadolescents: examining efficacy and potential treatment mechanisms. Journal of the American Academy of Child and Adolescent Psychiatry, 54(3), 191 - 199. https://doi.org/10.1016/j.jaac.2014.12.011

[38] Kornstein, S. G., Schatzberg, A. F., Thase, M. E., Yonkers, K. A., McCullough, J. P., Keitner, G. I., Gelenberg, A. J., Ryan, C. E., Hess, A. L., Harrison, W., Davis, S. M., & Keller, M. B. (2000). Gender differences in chronic major and double depression. Journal of affective disorders, 60(1), 1 - 11. https://doi.org/10.1016/s0165-0327(99)00158-5

[39] Moreno, F. A., McGahuey, C. A., Freeman, M. P., & Delgado, P. L. (2006). Sex differences in depressive response during monoamine depletions in remitted depressive subjects. The Journal of clinical psychiatry, 67(10), 1618 - 1623. https://doi.org/10.4088/jcp.v67n1019

[40] Nishizawa, S., Benkelfat, C., Young, S. N., Leyton, M., Mzengeza, S., de Montigny, C., Blier, P., & Diksic, M. (1997). Differences between males and females in rates of serotonin synthesis in human brain. Proceedings of the National Academy of Sciences of the United States of America, 94(10), 5308 - 5313. https://doi.org/10.1073/pnas.94.10.5308

[41] Young, S. N., Gauthier, S., Anderson, G. M., & Purdy, W. C. (1980). Tryptophan, 5-hydroxyindoleacetic acid and indoleacetic acid in human cerebrospinal fluid: interrelationships and the influence of age, sex, epilepsy and anticonvulsant drugs. Journal of neurology, neurosurgery, and psychiatry, 43(5), 438 - 445. https://doi.org/10.1136/jnnp.43.5.438

[42] Staley, J. K., Krishnan-Sarin, S., Zoghbi, S., Tamagnan, G., Fujita, M., Seibyl, J. P., Maciejewski, P. K., O'Malley, S., & Innis, R. B. (2001). Sex differences in 123I-beta-CIT SPECT measures of dopamine and serotonin transporter availability in healthy smokers and nonsmokers. Synapse (New York, N.Y.), 41(4), 275 - 284. https://doi.org/10.1002/syn.1084

[43] Cidis Meltzer, C., Drevets, W. C., Price, J. C., Mathis, C. A., Lopresti, B., Greer, P. J.,
Villemagne, V. L., Holt, D., Mason, N. S., Houck, P. R., Reynolds, C. F., 3rd, & DeKosky, S. T. (2001). Gender-specific aging effects on the serotonin 1A receptor. Brain research, 895(1-2), 9 - 17. https://doi.org/10.1016/s0006-8993(00)03211-x

[44] Legato M. J. (1997). Gender-specific physiology: how real is it? How important is it? International journal of fertility and women's medicine, 42(1), 19 - 29.

[45] Veral, A., Alper, G., Mentes, G., & Ersöz, B. (1997). Age and sex related alterations in serum and platelet monoamine oxidase. European journal of clinical chemistry and clinical biochemistry: journal of the Forum of European Clinical Chemistry Societies, 35(4), 265 - 268.

[46] Laakso, A., Vilkman, H., Bergman, J., Haaparanta, M., Solin, O., Syvälahti, E., Salokangas, R. K., & Hietala, J. (2002). Sex differences in striatal presynaptic dopamine synthesis capacity in healthy subjects. Biological psychiatry, 52(7), 759 - 763. https://doi.org/10.1016/s0006-3223(02)01369-0

[47] Lewinsohn, P. (1974). A behavioral approach to depression. In R. J. Friedman, & M. M. Katz (Eds.), Psychology of depression: Contemporary theory and research (pp. 157 – 185). Oxford, England: John Wiley & Sons.

[48] Beck, A. T., Rush, A. J., Shaw, B. F., & Emery, G. (1979). Cognitive therapy of depression. New York: Guilford.

[49] Dimidjian, S., Hollon, S. D., Dobson, K. S., Schmaling, K. D., Kohlenberg, R. J., Addis, M. E., et al. (2006). Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. Journal of Consulting and Clinical Psychology, 74, 658 - 670, doi:10.1037/0022-006X.74.4.658.

[50] Dunlop, B. W., Binder, E. B., Cubells, J. F., Goodman, M. M., Kelley, M. E., Kinkead, B., ..., & Mayberg, H. S. (2012). Predictors of remission in depression to individual and combined treatments (PReDICT): study protocol for a randomized controlled trial. Trials, 13(1), 1-18.

[51] Ritschel, L. A., Ramirez, C. L., Cooley, J. L., & Edward Craighead, W. (2016). Behavioral activation for major depression in adolescents: Results from a pilot study. Clinical Psychology: Science and Practice, 23(1), 39-57.

[52] Coffman, S. J., Martell, C. R., Dimidjian, S., Gallop, R., & Hollon, S. D. (2007). Extreme nonresponse in cognitive therapy: Can behavioral activation succeed where cognitive therapy fails? Journal of Consulting and Clinical Psychology, 75, 531 - 541. doi:10.1037/0022-006X.75.4.531.

[53] Dimidjian, S., Barrera Jr, M., Martell, C., Muñoz, R. F., & Lewinsohn, P. M. (2011). The origins and current status of behavioral activation treatments for depression. Annual review of clinical psychology, 7, 1-38.

[54] Martell, C. R., Addis, M. E., & Jacobson, N. S. (2001). Depression in context: Strategies for guided action. New York: Norton.

[55] Dimidjian, S., Martell, C. R., Addis, M. E., & HermanDunn, R. (2008). Behavioral activation for depression. In D. H. Barlow (Ed.), Clinical handbook of psychological disorders (pp. 328 – 364). New York, NY: Guilford Press.

[56] Mayberg, H. S. (2003). Modulating dysfunctional limbic-cortical circuits in depression: Towards development of brain-based algorithms for diagnosis and optimised treatment. British Medical Bulletin, 65, 193 - 207. doi:10.1093/bmb/65.1.193.