

Case Report

Current Severe Depressive Episode in Bipolar II Disorder with Anxious Distress and Post-traumatic Stress-Disorder with Derealization: a Case Report

Muhammad Alim Jaya^{1,2} , Andi Jihan Nashila Haris³, Andi Karlina Syahrir⁴

¹Department of Psychiatry, Faculty of Medicine, Moslem University of Indonesia, Makassar 90231, Indonesia.

²Department of Psychiatry, Faculty of Medicine, Hasanuddin University, Makassar 90245, Indonesia.

³Faculty of Medicine, Hasanuddin University, Makassar 90245, Indonesia.

⁴Faculty of Medicine, Muhammadiyah University, Makassar 90221, Indonesia.

Abstracts

Received: March 27, 2023

Accepted : July 15, 2024

Published Online : November 1, 2024

You are free to:

Share — copy and redistribute the material in any medium or format

Adapt — remix, transform, and build upon the material for any purpose, even commercially.

The licensor cannot revoke these freedoms as long as you follow the license terms.

Correspondence Author:

Email: alimjayam@gmail.com

Introduction: Bipolar II disorder experiences more frequent episodes of depression and is sometimes comorbid with post-traumatic stress disorder (PTSD). However, there is no clear method to distinguish between depression induced by bipolar disorder and PTSD. Through this case, we aim to examine the features of the patient's bipolar disorder and PTSD from the depressive episodes.

Case: A 23-year-old Indonesian woman came with the chief complaint of unexplainable discomfort that had been experienced almost daily for the past two weeks. The patient also complained that she was often lonely. Patients did not get adequate parenting from her parents, so patients have unfavorable relationships with her family. In addition, patients previously experienced sexual harassment that caused severe trauma. She was diagnosed with a current severe depressive episode in bipolar II disorder with anxious distress and PTSD. **Discussion:** Bipolar disorder is frequently comorbid with PTSD. She was given Sertraline 25 mg once daily, Aripiprazole 5 mg twice a day, Clobazam 5 mg once a day at night, Folic acid 400 mcg once a day, and psychotherapy. After four weeks of treatment, there was an improvement in symptoms by a decrease in the HDRS and the HARS scores. **Conclusion:** In the case presented, bipolar patients have major complaints related to somatic symptoms accompanied by a history of experiencing severe traumatic events. Thus, bipolar patients do not always come with the chief complaint of mood swings. Furthermore, these complaints improved with the combination of anti-psychotic, anti-depressant, anti-anxiety, and psychotherapy.

Keywords: Bipolar Disorder, Posttraumatic Stress Disorder, Depressive, Mood Disorder, Mental Health

Cite this as: Jaya. M. A., Haris. A. J. A., Syahrir. A. K. "Current Severe Depressive Episode in Bipolar II Disorder with Anxious Distress and Post-traumatic Stress-Disorder with Derealization: a Case Report". Jurnal Psikiatri Surabaya, vol. 13, no. 2, pp.197-205, 2024. doi: [10.20473/jps.v13i2.44355](https://doi.org/10.20473/jps.v13i2.44355)

INTRODUCTION

Bipolar II disorder is a chronic mental illness and is found quite often. Bipolar II is characterized by multiple episodes of major depressive disorder and episodes of hypomania [1]. Approximately 50% of patients with major depressive disorder have bipolar II disorder, although hypomania can sometimes develop at the end of a depressive episode and in most bipolar II [2]. Hypomania is a lower state of a manic episode compared to mania. Hypomania does not last long; it only lasted a few days in a week or a month [1]. Another form of bipolar II disorder is major depression, which overlaps with cyclothymia. Hypomania might precede or follow a major depressive episode. Each period between episodes might be characterized by cyclothymic disturbances [3]. Furthermore, the prevalence of bipolar disorder generally ranges from 3–10 cases per 100,000 population annually globally, and the lifetime prevalence is estimated to be around 3–7%. Bipolar disorder is also frequently comorbid with other psychiatric disorders, including post-traumatic stress disorder (PTSD) [4, 5]. PTSD is a stress-related disorder following a trauma defined by re-experiencing, avoidance, negative beliefs, and symptoms of increased alertness in survivors of a severe traumatic event [6, 7]. PTSD is a common outcome after a variety of traumatic events, from long-lasting events (such as kidnapping and physical abuse) to shorter events (such as accidents) [5]. Furthermore, the prevalence of PTSD, according to the survey of The United States National Comorbidity, reported that from 5877 cases, >60% are men and >50% are women who had been exposed to traumatic events in the age group of 15–54 years. Meanwhile, the lifetime prevalence of PTSD was found to occur in >10% of women and >5% of men. Moreover, there is a 50% chance of remission within 2 years [8].

Based on the results of studies in community groups, outpatients and inpatients provide evidence of an increase in PTSD rates in

patients with bipolar disorder. However, for patients diagnosed with bipolar II disorder and PTSD, there is no clear method to distinguish whether the depression or the anxiety induced by bipolar disorder or attacks of PTSD. In this case report, we describe a patient diagnosed with bipolar II disorder and PTSD who presented to the writers during a depressive episode. Through this case, we aim to examine the features of the patient's bipolar disorder and PTSD from the depressive episodes and discuss them based on the relevant literature.

CASE

A 23-year-old Indonesian woman came with the chief complaint of unexplainable discomfort and symptoms of anxiety, including heart palpitations, cold sweats, and sweaty palms that had been experienced almost daily for the past two weeks. The complaint worsens, especially when having many thoughts or remembering unpleasant past events. The patient also sometimes suddenly complained of shortness of breath, heartburn, and abdominal pain, such as dysmenorrhea, when experiencing anxiety. The patient was worrisome if these physical complaints came suddenly and made the patient always introspective.

The patient also complained that she often felt empty and lonely, thinking that no one cared and wanted to be friends with her. She even felt that her best friends were avoiding her. This made the patient shut herself and vent her feelings by crying and shouting. The patient also avoided talking to her family and other people because she felt that no one was there to support her. Therefore, the patient did not have friends to share her worries, especially the severe problems faced by the patient.

At the age of 20 years, the patient was admitted to the emergency room several times due to heartburn caused by excessive anxiety and sadness, followed by frequent crying and loneliness. Following the event, the patient had regular check-ups with a psychiatrist for

6 consecutive months and felt improvement, so the patient stopped going to a psychiatrist for control.

At the age of 13 years, the patient experienced sexual harassment. Not long after the incident, the patient was admitted to the hospital with complaints of shortness of breath and abdominal pain. This made the patient experience severe trauma that was felt until the present. The patient still often remembered the incident now. On top of that, the patient was sensitive when hearing words related to 'sexual harassment'. Patients also often had nightmares. Then, the patient re-entered the hospital several times with the same complaints. Therefore, the patient felt anticipatory anxiety, for fear that these complaints could appear suddenly.

On the mental status examination, we found a woman of medium height, sitting quietly in front of the examiner. The patient's face looked age-appropriate and looked well-groomed. Self-care was considered well. She was completely aware (*compos mentis*), had a quite calm psychomotor, slightly slowed body movements, often seemed to clench her hands during the interview, and moved her right hand to the left or vice versa. The patient occasionally showed her currently wet palms. Her speech was quite spontaneous, sometimes slowed down, and with normal intonation. Her attitude towards the examiners was cooperative. On the affective examination, an appropriate dysphoric mood with depressive affect was found and could be empathized with. It was found that there was a disturbance in self-perception and experience in the form of derealization, in which the patient sometimes felt that she was not real, like a dream. In the thought process, sufficient productivity, relevant, coherent, and no language impairment was found, thoughts in the form of preoccupation with incidents of sexual abuse in the past and fear of attacks of shortness of breath that could come at any time suddenly, and some irrational ideas in the form of labeling, jumping to conclusions, and also the suspicious idea

that her best friends were avoiding her. The patient had good impulse control during the interview. The patient had a grade 5 insight and a level of trustworthiness.

On physical examination, the patient's nutritional status was good, and internal and neurological examinations were within normal limits. Initial psychometric examination revealed a score of Hamilton Depression Rating Scale (HDRS): Score 26, Hamilton Anxiety Rating Scale (HARS): Score 21, MINI-International Classification of Diseases (ICD)-10: panic disorder, PTSD, recurrent depressive episode disorder, dysthymia, and no risk of suicide. Based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [6], she was diagnosed with a current severe depressive episode in bipolar II disorder with anxious distress and post-traumatic stress disorder with derealization.

The initial treatment for this patient was psychopharmacotherapy, including Sertraline, Aripiprazole, Clobazam, and Folic acid. Sertraline 25 mg was given once a day in the morning to improve her mood. Aripiprazole 5 mg was given twice a day in the morning and evening for complaints of derealization, and Clobazam 5 mg once a day at night for complaints of anxiety. Folic acid 400 mcg once a day was given to inhibit the decline in cognitive function. Patients also had received psychotherapy.

After four weeks of treatment, there was an improvement in symptoms, marked by a decrease in the HDRS score of 12 and the HARS score of 8, and there was no more derealization felt by the patient. Subsequently, the sertraline was discontinued, and the patient was given a mood stabilizer, namely valproic acid 250 mg twice daily.

DISCUSSION

In this case, the patient was diagnosed with bipolar II affective disorder and a current severe depressive episode without psychotic symptoms after being preceded by one episode of hypomania and a previous cyclothymic condition. The course of the patient's

disease to a severe condition at this time was due to multifactorial results. The depressive episode experienced by the patient is the result of a narcissistic injury experienced by the patient while undergoing school and lecture burden [5]. Based on the theory of self-psychology from Heinz Kohut [9, 10], depressive mood in individuals who have narcissistic vulnerability is associated with chronic feelings of emptiness as a response to traumatic events in parenting styles with a lack empathy. Where the patient's affective or emotional experiences in childhood are not sensitively responded to by parents and family, the need for mirroring in patients is not fulfilled. Thus, patients become too lazy to tell their problems and conditions to their parents or families. Meanwhile, the patient's feelings of sadness that arise in certain conditions must be faced alone without adequate empathy from close relations. In other words, the patient is left alone with her affective experiences and feels emotionally empty.

When the patient starts trying to develop the idealized parental image, the ideal father and mother figures are not visible because of the busyness of her parents. Patients mostly live with their aunts and grandmothers, so there is less interaction with parents. This actually makes the patient experience a disappointment for his parents. Patients actually really hope to get attention from her parents and get praise when they excel in academics. Therefore, the patient seems to lack emotional ties with her father and mother. The experience of disappointment in admiring adult figures (parents) and idealized parental imago finally persists in the patient as part of the self-object that she needs to maintain narcissistic homeostasis [11, 12]. Based on this disappointment, the patient struggles to fill the void in herself emotionally by looking for someone else to idealize and identify with her. Furthermore, the patient establishes a close relationship with her grandmother. And when her grandmother passed away, it caused the patient to be devastated and very

sad. Because the existence of a grandmother when living as an idealized image gives a sense of loss to the patient.

Failure to fulfill the needs of mirroring and idealized parental imago in childhood hinders the formation of self-worth, self-regard, and a sense of wholeness in patients. What happens to patients is deficient self, which is very susceptible to self fragmentation. This self-fragmentation condition makes the patient always want to do their best to gain better recognition and acceptance from those around them [11]. Through this pattern, the patient's personality develops towards a narcissistic personality trait.

According to her personality traits and narcissistic needs that are hidden in the patient's deepest desires, it can be seen that in the patient's life, several times the patient's decreased mood or depressive condition is the result of a narcissistic injury that occurs [11, 12]. In these conditions, the patient receives considerable pressure and is not in a state of constant support from others to maintain her ego. Moreover, in the formation of object relations, the patient places the object as a sub-organization of the ego, where the meaning of her life depends on the identification of the ego aspects of an object. The object in this case is the support of others for the achievements made by the patient. So that when the need for this support does not exist, or in certain situations the patient actually gets criticism and rejection, then this destroys the patient's realistic self-esteem and the patient's self-integrity feels lost.

At the time of entering high school, the patient experienced culture shock because of the different atmosphere in junior high school. Patients feel unable to compete with friends who are considered smarter than her and unable to establish close relationships with her friends. Patients with the somatization defense that was often used at that time often experienced heartburn and menstrual pain. The patient at that time experienced a narcissistic injury and then entered a depressed state, which in the end the patient

escaped from by joining a student organization. The patient also had difficulties at that time and with projection defense, where the patient said that the teacher who was not involved in teaching made her unable to compete with her friends. Furthermore, patients carry out suppression of defense, but this cannot be borne by the patient's ego, so patients tend to carry out repression more often when undergoing education and daily life.

The patient had been abused when she was in junior high school. After the patient is abused, the patient feels guilty and feels "dirty." Since then, when the patient violates the rules that have been set or is under pressure, there is often a feeling of worry in the patient because they feel inferior, causing feelings of avoidance anxiety by trying to avoid the source of stress [13]. According to Freud, anxiety is seen as a psychic conflict between the sexual unconscious or the suppression of the aggressive desires of the id and the threat of punishment from the superego. Anxiety is understood as a signal of danger from the subconscious. In response to these signals, the ego forms defense mechanisms to prevent unacceptable thoughts and feelings from rising into alertness. When anxiety signals fail to compensate for activated ego defensive resources, persistent anxiety or other neurotic symptoms develop. Freud distinguished three kinds of anxiety, namely reality anxiety, neurotic anxiety, and moral anxiety. Reality anxiety is an anxiety that stems from the fear of threatening dangers in the real world. Neurotic anxiety is anxiety or fear of being punished for exhibiting impulsive behavior that is dominated by the id. Moral anxiety explains how the superego develops; usually, individuals with strong consciences will experience more intense conflict than individuals who have conditions of looser moral tolerance. According to Freud, neurosis occurs because the repression mechanisms that have been used by patients are no longer effective, so that impulses that have been repressed and are in the unconscious will en-

ter consciousness, which causes anxiety as a conscious signal of danger. In responding to these ego signals, the patient mobilizes other defense mechanisms, such as sublimation, to prevent unacceptable thoughts and feelings from appearing in consciousness [14]. After the defense mechanism is no longer effective, there will be complaints of autonomic hyperactivity that interferes with daily activities and functions.

Based on the stress-diathesis model, the psychopathology experienced by the patient was an interaction between stress factors and diathesis (vulnerability) [15]. The stress factors in this current patient include interpersonal relationship problems with family in which ineffective communication occurred with her parents and family, as well as the painful psychological traumatic experience of an event that was perceived as a failure according to the patient's ego. Meanwhile, the diathesis factor in the current patient is epigenetic factors formed from parenting that cause traumatic disappointments in the patient's childhood [15, 16]. Other factors were also the personality traits of the patient with limited coping mechanisms and immature defense mechanisms, as well as affective distortion that is not in line with the patient's cognitive [16]. Thus, the interaction of diathesis, or the patient's vulnerability to social stress and psychosocial stress experience, makes the patient ultimately experience a mental disorder.

Along the way, the patient experienced sexual abuse as a teenager, which causes the patient to experience traumatic stress. PTSD is a common outcome after a variety of traumatic events, from kidnapping and torture to shorter events, such as accidents. Horowitz's theory states that memories of a traumatic event occur constantly in a person's mind and are so painful that they consciously suppress it (through distraction) or repress it [17]. The person is believed to have experienced some kind of internal struggle to integrate the trauma into his or her beliefs about himself or herself and the world in or-

der to accept it sensibly. In other words, the awakening of memories of previous experiences gives rise to a psychological conflict [17, 18]. This creates a feeling of discomfort that repeats itself in the patient but was successfully suppressed, and the emergence of aggressive impulses was successfully repressed. When the patient experienced these events, the patient did not have a close relationship with anyone to share with. This was enough to hit the patient's internal balance, so the patient became uncomfortable and lost interest in daily activities.

Initial treatment for this patient includes psychopharmacotherapy, namely Sertraline, Aripiprazole, Clobazam, and folic acid. Sertraline is an antidepressant from the serotonin selective reuptake inhibitor (SSRI) drug class that has the fewest gastrointestinal side effects. Sertraline is an antidepressant with a major inhibitory effect on presynaptic serotonin reuptake. This inhibition of serotonin reuptake results in the accumulation of serotonin [19]. Serotonin in the central nervous system plays a role in regulating mood, personality, and wakefulness, which is why blocking serotonin reuptake is beneficial in disorders such as major depression [20]. Sertraline also has minimal effects on norepinephrine and dopamine uptake, and studies have shown that it has more dopaminergic activity than other drugs in the same SSRI class. Sertraline's mechanism of action makes it highly effective when used in the treatment of various psychiatric conditions. Apart from major depression, the Food and Drug Administration of the United States also approved the indications for sertraline for the treatment of obsessive-compulsive disorder, panic disorder, PTSD, premenstrual dysphoric disorder, and social anxiety disorder [21], and the initial dose is 25 mg once daily [19]. The dose of sertraline is increased by 50 mg gradually at weekly intervals to a maximum of 200 mg per day. The dose of Sertraline is generally once daily, and administration can be done any time of day [19, 22]. Furthermore, it is very important

to monitor for unusual changes in behavior, anxiety, suicidality, or other clinical signs of worsening disease in the patient. However, regular evaluation for depression and suicidality, especially when changing the dose of sertraline, is required. Sertraline can also trigger mania in patients at risk for bipolar disorder [19, 23]. Manic symptoms should be monitored regularly in patients starting Sertraline, especially if they have a family history of mania or bipolar disorder [19].

In the administration of Sertraline, the therapeutic effect will only start to appear by the second week, so that at the beginning of therapy, it can be given together with anti-anxiety drugs to overcome complaints of anxiety, somatization, and panic attacks in patients [24]. These complaints of somatization and panic attacks are the result of anxiety from this patient's inner unconscious. The major anxiety-related neurotransmitters in the limbic region are norepinephrine, gamma-aminobutyric acid (GABA), and serotonin [25]. The benefit of treating anxiety with bipolar disorder comorbid with benzodiazepines is implicated in GABA, which plays a role in the pathophysiology of anxiety disorders [26]. Clobazam is a high-potency benzodiazepine drug that has been shown to be very effective because it has a rapid onset of action [27]. Clobazam is given to the patient initially for 4-6 weeks, after which the dose will be gradually reduced until finally discontinued. Thus, it is very helpful at the start of therapy or when a rapid onset of therapeutic effect is required.

Aripiprazole is a new antipsychotic that was originally approved for the treatment of schizophrenia and has been shown to be effective in bipolar disorder. This drug is well studied, as randomized controlled trials have been conducted in different phases of bipolar disorder [28]. Aripiprazole exhibits pharmacodynamic properties of partial agonism, functional selectivity, and serotonin-dopamine activity [29]. A previous study reported that aripiprazole significantly reduced depressive symptoms at the start of treatment,

and the results were not significantly different from the placebo at the 8th week primary endpoint. For long-term treatment, Aripiprazole was superior to placebo in delaying the time to relapse for manic episodes but not for depressive episodes after 26 and 100th weeks of maintenance therapy [30].

The patient is also given folic acid to inhibit the decline in cognitive function that might be caused by antipsychotics or antidepressants. Folic acid (an artificial chemical analog of natural folate) is a member of the B vitamin family. It is important for the functioning of the nervous system at all ages. Folic acid helps in improving memory status by reducing oxidative stress and maintaining the integrity of neurons [31]. Based on previous studies, it was reported that the administration of folic acid supplements to patients with mild cognitive impairment for 12 months can significantly improve cognitive performance and reduce peripheral inflammatory cytokine levels [32].

Four weeks of treatment, there was an improvement in symptoms, marked by a decrease in the HDRS and the HARS scores, and there was no more derealization felt by the patient. Subsequently, sertraline was discontinued, and the patient was given a mood stabilizer, namely valproic acid, to keep the patient's mood stabilized.

The psychotherapy given to these patients included supportive psychotherapy, namely ventilation and reassurance, as well as cognitive behavioral therapy [33]. Supportive psychotherapy in these patients aims to support and strengthen ego functions and expand the defense mechanisms she has with new and better ones, as well as improvement to a state of balance that is more adaptive. Cognitive behavioral therapy with rationale emotional behavior therapy to rebuild mindsets (attitudes, assumptions, and beliefs), test mindsets, identify feelings, and decide what is useful and what is not beneficial for patients, so that she can build a more productive way of thinking and improve quality of life in patients.

CONCLUSION

In patients with concomitant episodes of bipolar II and PTSD, there are currently no clear guidelines for distinguishing the origin of the depressive episode. Patients have major complaints related to somatic symptoms accompanied by a history of experiencing severe traumatic events. Thus, bipolar patients do not always come with the chief complaint of mood swings. In the present case, the complaints related to mood are additional complaints. However, it is important to attempt to distinguish the underlying cause of depressive episodes through detailed patient history, neurological examination, and neuroimaging, as this can influence future treatment plans. Furthermore, the combination of anti-psychotic, anti-depressant, anti-anxiety, and psychotherapy could improve the symptoms in this patient. In addition, in the case presented, bipolar II and PTSD occur in children aged to adolescence, which might be a clue for further investigation in the future.

ACKNOWLEDGEMENT

None

FUNDING

There are no financial support and sponsorship related to this work.

CONFLICT OF INTEREST

The authors report no conflicts of interest.

REFERENCES

- [1] F. Benazzi, "Bipolar II Disorder," *CNS Drugs*, vol. 21, no. 9, pp. 727–740, 2007, doi: [10.2165/00023210-200721090-00003](https://doi.org/10.2165/00023210-200721090-00003).
- [2] M. M. C. Wong, "Management of Bipolar II Disorder," *Indian J. Psychol. Med.*, vol. 33, no. 1, pp. 18–28, Jan. 2011, doi: [10.4103/0253-7176.85391](https://doi.org/10.4103/0253-7176.85391).
- [3] T. Singh and M. Rajput, "Misdiagnosis of bipolar disorder.," *Psychiatry (Edgmont)*, vol. 3, no. 10, pp. 57–63, Oct. 2006, [Online]. Available: <http://www.ncbi.nlm.nih.gov/pubmed/20877548>.

- [4] J. M. Cerimele, A. M. Bauer, J. C. Fortney, and M. S. Bauer, "Patients With Co-Occurring Bipolar Disorder and Posttraumatic Stress Disorder," *J. Clin. Psychiatry*, vol. 78, no. 5, pp. e506–e514, May 2017, doi: [10.4088/JCP.16r10897](https://doi.org/10.4088/JCP.16r10897).
- [5] B. J. Sadock, V. A. Sadock, Kaplan and Sadock's synopsis of psychiatry: Behavioral sciences/clinical psychiatry, 2th ed. Penerbit Buku Kedokteran EGC, 2004. pp. 197-217
- [6] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Association, 2013. pp. 132-139
- [7] J. I. Bisson, "Post-traumatic stress disorder," *Occup. Med. (Chic. Ill.)*, vol. 57, no. 6, pp. 399–403, Aug. 2007, doi: [10.1093/occ-med/kqm069](https://doi.org/10.1093/occ-med/kqm069).
- [8] R. C. Kessler, "Posttraumatic Stress Disorder in the National Comorbidity Survey," *Arch. Gen. Psychiatry*, vol. 52, no. 12, p. 1048, Dec. 1995, doi: [10.1001/arch-psyc.1995.03950240066012](https://doi.org/10.1001/arch-psyc.1995.03950240066012).
- [9] Baker HS, Baker MN. Heinz Kohut's self psychology: an overview. *Am J Psychiatry*. 1987 Jan;144(1):1-9. doi: [10.1176/ajp.144.1.1](https://doi.org/10.1176/ajp.144.1.1). PMID: 3541648.
- [10] Goldberg A. Self psychology since Kohut. *Psychoanal Q*. 1998 Apr;67(2):240-55. PMID: 9577856.
- [11] Mollon P. Narcissistic vulnerability and the fragile self: a failure of mirroring. *Br J Med Psychol*. 1986 Dec;59 (Pt 4):317-24. doi: [10.1111/j.2044-8341.1986.tb02700.x](https://doi.org/10.1111/j.2044-8341.1986.tb02700.x). PMID: 3801340.
- [12] Gabbard GO. Narcissism and suicide risk. *Ann Gen Psychiatry*. 2022 Jan 22;21(1):3. doi: [10.1186/s12991-022-00380-8](https://doi.org/10.1186/s12991-022-00380-8). PMID: 35065658; PMCID: PMC8783517.
- [13] Schulte HM, Hall MJ, Crosby R. Violence in patients with narcissistic personality pathology: observations of a clinical series. *Am J Psychother*. 1994 Fall;48(4):610-23. doi: [10.1176/appi.psychotherapy.1994.48.4.610](https://doi.org/10.1176/appi.psychotherapy.1994.48.4.610). PMID: 7872421.
- [14] Pizarro Obaid F, De la Fabián R. The phylogenetic argument in Freud's metapsychology of anxiety. *Int J Psychoanal*. 2022 Oct;103(5):806-827. doi: [10.1080/00207578.2022.2089571](https://doi.org/10.1080/00207578.2022.2089571). PMID: 36200360.
- [15] C. Goh and M. Agius, "The stress-vulnerability model how does stress impact on mental illness at the level of the brain and what are the consequences?," *Psychiatr. Danub.*, vol. 22, no. 2, pp. 198–202, Jun. 2010, [Online]. Available: <http://www.ncbi.nlm.nih.gov/pubmed/20562747>.
- [16] M. Oh, J.-W. Kim, N.-H. Yoon, S. A. Lee, S. M. Lee, and W. S. Kang, "Differences in Personality, Defense Styles, and Coping Strategies in Individuals with Depressive Disorder According to Age Groups Across the Lifespan," *Psychiatry Investig.*, vol. 16, no. 12, pp. 911–918, Dec. 2019, doi: [10.30773/pi.2019.0160](https://doi.org/10.30773/pi.2019.0160).
- [17] D. Berntsen, D. C. Rubin, and M. K. Bohni, "Contrasting models of posttraumatic stress disorder: Reply to Monroe and Mineka (2008).," *Psychol. Rev.*, vol. 115, no. 4, pp. 1099–1106, Oct. 2008, doi: [10.1037/a0013730](https://doi.org/10.1037/a0013730).
- [18] D. C. Rubin, A. Boals, and D. Berntsen, "Memory in posttraumatic stress disorder: Properties of voluntary and involuntary, traumatic and nontraumatic autobiographical memories in people with and without posttraumatic stress disorder symptoms.," *J. Exp. Psychol. Gen.*, vol. 137, no. 4, pp. 591–614, 2008, doi: [10.1037/a0013165](https://doi.org/10.1037/a0013165).
- [19] H. K. Singh and A. Saadabadi, Sertraline, In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. pp. 1-16
- [20] M. J. Robson, M. A. Quinlan, and R. D. Blakely, "Immune System Activation and Depression: Roles of Serotonin in the Central Nervous System and Periphery," *ACS Chem. Neurosci.*, vol. 8, no. 5, pp. 932–942, May 2017, doi: [10.1021/acschemneuro.6b00412](https://doi.org/10.1021/acschemneuro.6b00412).
- [21] R. M. A. Hirschfeld, "Sertraline in the treatment of anxiety disorders," *Depress. Anxiety*, vol. 11, no. 4, pp. 139–157, 2000, doi: [10.1002/1520-6394\(2000\)11:4<139::AID-](https://doi.org/10.1002/1520-6394(2000)11:4<139::AID-)

DA1>3.0.CO;2-C.

[22] S. H. Preskorn and R. M. Lane, "Sertraline 50 mg daily: the optimal dose in the treatment of depression," *Int. Clin. Psychopharmacol.*, vol. 10, no. 3, pp. 129–141, Sep. 1995, doi: [10.1097/00004850-199510030-00001](https://doi.org/10.1097/00004850-199510030-00001).

[23] R. Patel et al., "Do antidepressants increase the risk of mania and bipolar disorder in people with depression? A retrospective electronic case register cohort study: Table 1," *BMJ Open*, vol. 5, no. 12, p. e008341, Dec. 2015, doi: [10.1136/bmjopen-2015-008341](https://doi.org/10.1136/bmjopen-2015-008341).

[24] G. Lewis et al., "The clinical effectiveness of sertraline in primary care and the role of depression severity and duration (PANDA): a pragmatic, double-blind, placebo-controlled randomised trial," *The Lancet Psychiatry*, vol. 6, no. 11, pp. 903–914, Nov. 2019, doi: [10.1016/S2215-0366\(19\)30366-9](https://doi.org/10.1016/S2215-0366(19)30366-9).

[25] I. Gauthier and P. Nuss, "Anxiety disorders and GABA neurotransmission: a disturbance of modulation," *Neuropsychiatr. Dis. Treat.*, p. 165, Jan. 2015, doi: [10.2147/NDT.S58841](https://doi.org/10.2147/NDT.S58841).

[26] C. A. Ott, "Treatment of anxiety disorders in patients with comorbid bipolar disorder," *Ment. Heal. Clin.*, vol. 8, no. 6, pp. 256–263, Nov. 2018, doi: [10.9740/mhc.2018.11.256](https://doi.org/10.9740/mhc.2018.11.256).

[27] D. Tolbert and F. Larsen, "A Comprehensive Overview of the Clinical Pharmacokinetics of Clobazam," *J. Clin. Pharma-*

col., vol. 59, no. 1, pp. 7–19, Jan. 2019, doi: [10.1002/jcph.1313](https://doi.org/10.1002/jcph.1313).

[28] A. Muneer, "The Treatment of Adult Bipolar Disorder with Aripiprazole: A Systematic Review," *Cureus*, Apr. 2016, doi: [10.7759/cureus.562](https://doi.org/10.7759/cureus.562).

[29] K. N. Fountoulakis, E. Vieta, and F. Schmidt, "Aripiprazole monotherapy in the treatment of bipolar disorder: A meta-analysis," *J. Affect. Disord.*, vol. 133, no. 3, pp. 361–370, Oct. 2011, doi: [10.1016/j.jad.2010.10.018](https://doi.org/10.1016/j.jad.2010.10.018).

[30] L. N. Yatham, "A clinical review of aripiprazole in bipolar depression and maintenance therapy of bipolar disorder," *J. Affect. Disord.*, vol. 128, pp. S21–S28, Jan. 2011, doi: [10.1016/S0165-0327\(11\)70005-2](https://doi.org/10.1016/S0165-0327(11)70005-2).

[31] R. Singh, S. S. Kanwar, P. K. Sood, and B. Nehru, "Beneficial Effects of Folic Acid on Enhancement of Memory and Antioxidant Status in Aged Rat Brain," *Cell. Mol. Neurobiol.*, vol. 31, no. 1, pp. 83–91, Jan. 2011, doi: [10.1007/s10571-010-9557-1](https://doi.org/10.1007/s10571-010-9557-1).

[32] F. Ma et al., "Effects of folic acid supplementation on cognitive function and Aβ-related biomarkers in mild cognitive impairment: a randomized controlled trial," *Eur. J. Nutr.*, vol. 58, no. 1, pp. 345–356, Feb. 2019, doi: [10.1007/s00394-017-1598-5](https://doi.org/10.1007/s00394-017-1598-5).

[33] Novick DM, Swartz HA. Evidence-Based Psychotherapies for Bipolar Disorder. *Focus (Am Psychiatr Publ)*. 2019 Jul;17(3):238-248. doi: [10.1176/appi.focus.20190004](https://doi.org/10.1176/appi.focus.20190004). Epub 2019 Jul 16. PMID: 32047369; PMCID: PMC6999214.