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HOW SLEEP DISTURBANCES AFFECT THOSE WITH BORDERLINE PERSONALITY DISORDER AND THE IMPLICATIONS FOR TREATMENT

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Abstract

This thesis argues that there is limited research on Borderline Personality Disorder's comorbidity with sleep disorders, and by pointing out the gaps in knowledge this will encourage researchers and doctors to consider this topic as important in the health care field. Sleep disorders can be anything from reduced total sleep time, fragmented sleep, and changes in sleep architecture, and all of these can cause and be caused by disruption of the circadian clock. There are various ways in which circadian clock disruption can cause diseases, cancer, and mental disorders through genes, sleep, and the environment. Borderline Personality Disorder comorbid with sleep disorders can cause a vicious cycle with one disorder increasing the other's intensity. These two disorders together can lead to higher rates of depressive, anxious, and suicidal symptoms. The current treatment options for BPD and sleep disturbances are limited and there is no standard way to treat these. With this being the case, we need to discover a way to treat both of these disorders in a patient without causing severe side effects and without ignoring one of the disorders altogether. Through a holistic view of a whole person through treatment plans that are specific to each individual, it is possible to alleviate some of the symptoms of BPD and sleep disorders, grant these people back a sense of control and self-autonomy over their lives, and strive towards the possibility of recovery.

Introduction

I decided to do my thesis on Borderline Personality Disorder (BPD) because I wanted to understand what a member of my family is going through. However I will not reveal their identity in this thesis, they are very near and dear to my heart, and I have full permission from them to discuss this topic. Ever since this person was diagnosed with BPD, I have constantly been thinking about what this means for them, for our family, for our future together, and for me. The past three years have been a whirlwind due to this weighing heavily on me since I have felt a need to do something about it. However nothing I do will make the diagnosis go away or cure this person, I have hoped that through learning more about it and reflecting deeply on what it means I can bring some peace to myself, my family, and this person. Dr. Stacy Chamberlin, my thesis advisor, told me that the biggest part of helping someone is to have conversations with them and try to understand who they are. This conversation, along with my curiosity for the science behind BPD, is what really sparked my passion for this project. Hopefully I can take this lesson from Dr. Chamberlin far beyond this thesis into my future relationships and into my future as a health care provider. I want to supplement my understanding of what this person is experiencing at the biochemical and psychological level, so I can discover how this disorder works in the body and what options there are for treatment.

This topic is very important to me because someone I love suffers from both BPD and sleep disturbances. I do want to acknowledge that my desire to find the best treatment method for BPD and sleep disturbances does come from a place of bias (however health care providers should have this biased desire for the best treatment), but I believe that my passion will only strengthen this thesis through the tenacity I have to learn and the great breadth of research I have done. Similarly, I know that there are many other lifestyle choices that affect BPD such as

exercise, diet, and relationships, but I wanted to focus on sleep due to it being the most interesting to me. Also, I wanted to have more quality research rather than quantity, so I needed to stick with only one aspect: sleep. I never thought much about sleep, as for me, sleep is not an issue. I realized that for some people, my family member included, it is a struggle every day to sleep, impacting all aspects of life. Throughout this thesis, I want to learn more about BPD comorbid with sleep disturbances. Moreover, I want to explain the biochemical pathways that affect BPD and sleep and compare and contrast different treatment methods for these two diseases. I hope by doing this in-depth research I can help others better understand the symptoms of BPD and how this affects the person suffering from this disorder and those around them. Additionally, I want to explore options for therapy, medication, and other sources of treatment so people will consider focusing on a holistic and personalized approach to medicine not only in mental disorders, but all health related diseases.

Borderline Personality Disorder comorbid with sleep disorders can cause a vicious cycle with one disorder increasing the other's intensity. These two disorders together can lead to higher rates of depressive, anxious, and suicidal symptoms (Fitzpatrick et al., 2021). With this being the case, we need to discover a way to treat both of these disorders in a patient without causing severe side effects and without ignoring one of the disorders altogether. Hopefully, by analyzing many different types of current treatment methods for BPD and sleep disorders (drugs, therapies, etc.), we can discover a way to effectively and cautiously treat both through personalized medicine. Additionally, there is not much research on BPD's comorbidity with sleep disorders to begin with and by pointing out the gaps in knowledge perhaps this will encourage researchers and doctors to consider this topic as an important topic in the health care field.

Chapter 1: Sleep

Section 1: How do genes affect sleep?

Sleep is an important part of existence for humans (ask anyone who has stayed up all night studying, traveling, or partying and then had to go about normal life the next day), as well as for all kinds of living organisms. Because of the importance of sleep, it must be a highly regulated process. The 24-hour circadian clock, which will be discussed in detail later, is genetically regulated by many different "clock genes" that control the rhythmic behavior in animals, plants, fungi, and bacteria (Patke et al., 2020). The fact that "clock genes" are in many different kingdoms of organisms means it is a vital part of being alive and maintaining life. This circadian clock relies on the transcriptional-translation feedback loop of these clock genes (Reinke & Asher, 2019). This process is highly regulated and influences the timing, quality, and duration of sleep cycles (Patke et al., 2020; Reinke & Asher, 2019). In fact, at least 20% of all mammalian genes are controlled by our "clock" (Benna et al., 2017). There are twelve core clock genes that are important in human circadian rhythm (Table 1; Benna et al., 2017). Through complex cell signaling, not all of which is understood, these clock genes are expressed.

Table 1: Information on the 12 core clock genes. The 12 core clock genes and their roles overall in relation to the circadian clock and sleep as well as their roles in cancer risk (Benna et al., 2017).

CLOCK (clock circadian regulator)	CLOCK (a possible "caretaker" gene) is located on chromosome 4 at 4q12 and is involved in growth arrest, DNA repair, chromatin remodeling, and apoptosis for UV radiated cells. Can contribute the most to overall cancer risk.
CSNK1E (casein kinase I epsilon)	CSNK1E is involved in phosphorylating other clock genes such as CRYs and PERs.
CRY1 (cryptochrome circadian clock 1)	CRY1 is located on chromosome 12 at 12q23-q24.1 and acts as a transcriptional repressor of other clock genes such as ARNTL and CLOCK. The inhibition of this gene leads to increased cancer risk.

CRY2 (cryptochrome circadian clock 2)	CRY2 is located on chromosome 11 at 11p11.2 and acts as a transcriptional repressor of other clock genes such as ARNTL and CLOCK. The inhibition of this gene leads to increased cancer risk.
PER1 (period circadian clock 1)	PER1 is located on chromosome 17 at 17q13.1 and is potentially involved as a tumor suppressor.
PER2 (period circadian clock 1)	PER2 is located on chromosome 2 at 2q37.3 and is potentially involved as a tumor suppressor.
PER3 (period circadian clock 1)	PER3 is located on chromosome 1 at 1p36.23 and is involved in
NPAS2 (neuronal PAS domain protein 2)	NPAS2 is located on chromosome 2 at 2q11.2 and is the largest human clock gene. This gene is involved as a transcription factor and as a potential tumor suppressor. Can contribute the most to overall cancer risk.
ARNTL (aryl hydrocarbon receptor nuclear like)	ARNTL can enhance gene expression as a protein complex with a few clock proteins.
RORA (RAR related orphan receptor A)	RORA is located on chromosome 15 at 15q21-q22 and potentially acts as a tumor suppressor gene. Can contribute the most to overall cancer risk.
NR1D1 (nuclear receptor subfamily 1 group D member 1)	NR1D1 suppresses the transcription of ARNTL and has been found to co-amplify with a receptor in HER2-positive breast cancer.
NR1D2 (nuclear receptor subfamily 1 group D member 2)	NR1D2 suppresses the transcription of ARNTL. There is a lack of data on this gene in particular.

One of the biggest pathways involves the CLOCK-ARNTL protein complex. This protein complex is able to stimulate the expression of PER and CRY, which negatively regulates the circadian rhythm (Oliveira et al., 2018). PER and CRY reach their peak expression at night and are able to inhibit the CLOCK-ARNTL heterodimer expression (Oliveira et al., 2018). In the morning, when CLOCK-ARNTL protein complex expression is low, it is unable to stimulate PER and CRY production, so they decrease while CLOCK-ARNTL expression increases (Figure 1; Oliveira et al., 2018). This CLOCK-ARNTL complex controls the expression of the clock genes and is able to create rhythmicity in the body (Oliveira et al., 2018). All this information may seem complicated, but essentially, differing levels of proteins are made available to the cells based on the timing of the circadian rhythm.

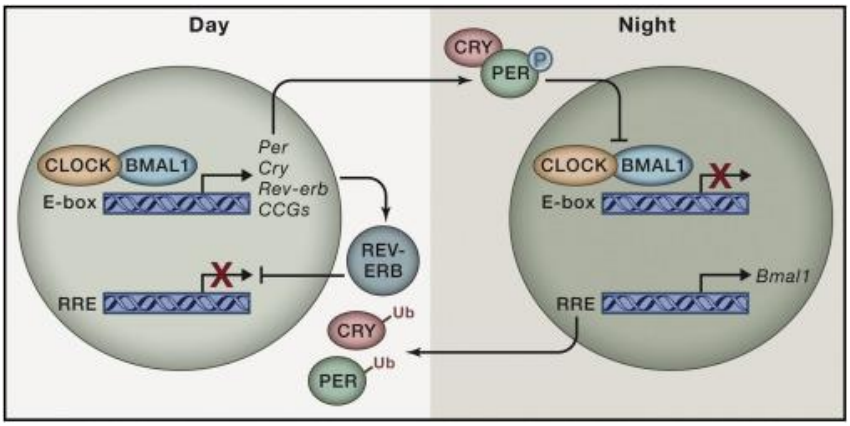

Figure 1. CLOCK and BMAL 1 activity during day versus night. Transcription factors including CLOCK and BMAL 1 control the transcription of genes during the day versus the night when they are repressed. Asher, G., & Sassone-Corsi, P. (2015). Time for food: the intimate interplay between nutrition, metabolism, and the circadian clock. *Cell*, *161*(1), 84–92. https://doi-org.dml.regis.edu/10.1016/j.cell.2015.03.015

This signaling pathway is very important since many of our organs and organ processes are controlled by clock genes. In fact, almost 40% of the genes in the kidneys are expressed under the control of the circadian rhythm; the kidneys are only rivaled by the genes in the liver (Reinke & Asher, 2019). The great importance of clock genes can be seen in Figure 2 where the transcription of clock genes is shown to affect organs and organ systems such as the heart, brain, pancreas, intestines, liver, muscle, and more (Figure 2; Guan & Lazar, 2021).

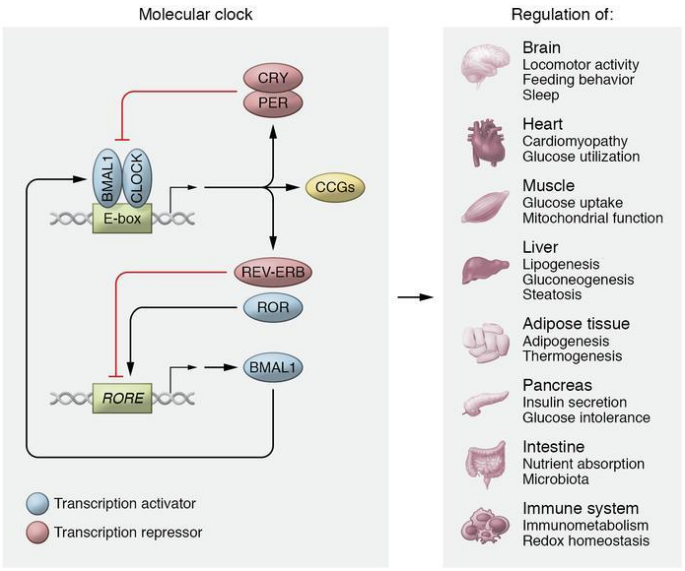

Figure 2. Molecular clock gene regulation of different organs. Gene transcription and the signal control over these genes affects the regulation of different organs and tissues. Guan, D., & Lazar, M. A. (2021). Interconnections between the circadian clock and metabolism. *The Journal of clinical investigation, 131*(15), e148278. https://doi-org.dml.regis.edu/10.1172/JCI148278

In order for this clock cycle to work, the genes need to be told when it is "night" and "day", so they can transcribe appropriately. The circadian rhythm must be able to adapt and respond to cues from outside and within using zeitgebers (cues that allow the circadian clock to adapt to the environment such as light and food) (Jagannath et al., 2017). These zeitgebers are able to modulate the expression of clock genes in order to change the molecular clockwork (Jagannath et al., 2017). Because of the body's ability to adapt the circadian clock to the environment, there can sometimes be issues with disruption or alteration of the "normal" rhythm. Reduced total sleep time, fragmented sleep, and changes in sleep architecture can all cause and be caused by disruption of the circadian clock (Jagannath et al., 2017). There are many mutations that have been found in circadian genes that not only affect sleep, but also have been associated with disease risk including cancer, diabetes, depression, and chronic sleep diseases (Oliveira et

al., 2018). Considering the gravity of those disease risks, one might understand why circadian genes and rhythm are so important.

Section 2: How the circadian clock works with hormones, environment, and other factors to influence sleep.

The circadian clock that was mentioned above is a very complicated process that helps us control our sleep/wake cycles. The intricate feedback loops that engage in gene expression and cell signaling are what generate the rhythms of a day that are called circadian (circa diem, 'about a day' in Latin) (Reinke & Asher, 2019). The reason organisms have evolved to have a 24-hour cycle was to adapt to the environmental changes caused by the Earth's rotation (Guan & Lazar, 2021). As we know, humans are more active during the day than the night and need hormones, proteins, and gene transcription to follow that pattern. The clock is controlled by a "pacemaker" that is located in the suprachiasmatic nuclei (SCN) in the hypothalamus (Albrecht, 2020). This SCN is made up about 20,000 neurons and acts as a pacemaker by controlling daily physiological hormone secretion and body temperature (Tähkämö et al., 2019). In fact, dopamine synthesis, the "happy" hormone, is under the control of the circadian clock (Albrecht, 2020). Dopamine is not the only reason that good quality sleep is important to happiness, as will be seen later on in this chapter.

If these complicated feedback loops do not seem like a big enough role, the circadian clock does even more! It also interacts with many other physiological systems including monoaminergic signaling (including dopamine), glutamatergic signaling, HPA axis function, metabolism, and immune function (Albrecht, 2020). These systems involve many different

organs that need clock regulation to function, as shown in Figure 2 (Patke et al., 2020). Examples of the circadian influence on physiology include glucose hemostasis in the liver and pancreas, wound healing by the skin, and ovulation signals by the ovaries (Patke et al., 2020). One of the most important organs for sleep regulation, the brain, is also affected by the circadian clock. The brain needs large amounts of energy to do its basic function, approximately 20% of the energy in the body, meaning that it will influence glucose regulation and be influenced by the circadian clock (Ketchesin et al., 2020). What is even more complex is that organs can undergo inter-organ crosstalk, which affects the rhythmic synthesis and excretion of hormones and other molecules (Reinke & Asher, 2019). The internal signals controlled by the circadian clock are extremely complicated and still not everything is known about how it all works.

While internal signals encompass many aspects of circadian rhythm, there are also many external signals as well. Entrainment is a process wherein the phase of the circadian rhythm is influenced and determined by environmental signals called zeitgebers (Patke et al., 2020). Light and food are two big examples of zeitgebers, and they are big contributors to circadian rhythm disruption in the modern world. These zeitgebers influence the circadian clock in different ways depending on the strength of the stimuli and what phase the circadian clock is in during the stimuli (Patke et al., 2020). Zeitgebers can delay or advance the circadian clock depending on the stimuli in order to line up with the solar day (Patke et al., 2020). Additionally, these zeitgebers can also have negative effects if the stimuli do not line up with the normal solar day. If the zeitgebers are random, especially during a stress experience, then the circadian clock may have trouble resynchronizing (Albrecht, 2020). Figure 3 shows the typical 24-hour circadian clock and what happens during certain sections of a 24-hour period (Figure 3). During the daytime section (fed state), there is highest alertness, coordination, strength, blood pressure, and blood

temperature (Zuker, 2021). During the nighttime section (fasting), there is the lowest body temperature, deepest sleep, and highest melatonin levels (Zuker, 2021). This can also be seen in Figure 2 (above) where all of the organs have important roles regarding sleep and are also heavily controlled by sleep. This is a very regulated process and disruptions in the external or internal environment can lead to alterations in this clock. Being a college student and researching this topic has really opened my eyes to the ways in which most of us are probably throwing off our circadian clocks: pulling all-nighters, being constantly stressed, and eating late at night!

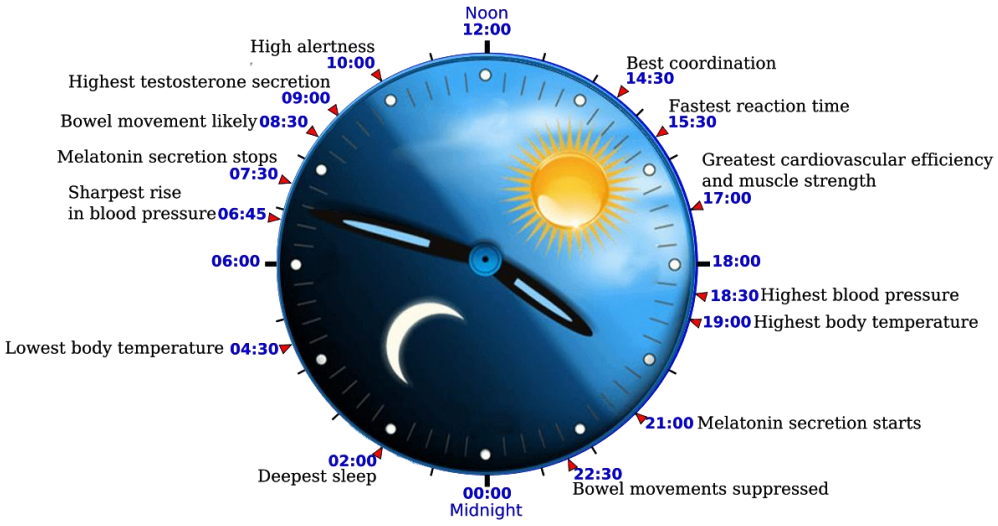

Figure 3. 24-hour circadian clock. This clock throughout the day showing times certain events happen. Zuker, H. (2021, January 29). *How to establish a healthy circadian rhythm*. Walalight. Retrieved March 16, 2022, from https://www.walalight.com/how-to-establish-a-healthy-circadian-rhythm/

External factors, such as light and food can greatly affect the circadian clock. Exposure to light at night can have a strong effect on the physiology in humans (Albrecht, 2020). This light can suppress melatonin and disrupt the glucocorticoid signaling, both of which disrupt the circadian clock function (Albrecht, 2020). Tähkämö et al. (2019) discovered that two hours of exposure to light in the evening suppressed melatonin. The exposure to this light (red or blue)

can shift the phase of the circadian rhythm of melatonin rapidly (Tähkämö et al., 2019). This shifting can cause issues with sleep and the entire circadian clock. This is why it is recommended for people to sleep in the dark without exposure to light. Bad news for those of us who are afraid of the dark (definitely not me).

Equally important, the timing of meals also impacts the circadian clock. Our eating habits and schedules are mostly dictated by our timing mechanisms (the circadian clock among others), however they are also affected by food availability, satiety, hunger, social habits, and convenience (Asher & Sassone-Corsi, 2015). Eating food outside of the normal time in which the circadian clock signals for food can lead to disruption of the clock processes. Meal timing can greatly impact our sleep/wake cycles, body temperature, performance, and alertness (Asher & Sassone-Corsi, 2015). All of this will lead to issues with sleep. Learning this makes me feel bad about all of the midnight mac-and-cheese and Taco Bell meals with my roommates. Knowing all of this, what exactly can happen when the circadian clock is disrupted or shifted, perhaps by eating a Crunchwrap Supreme at 1:00 a.m.?

Section 3: How can unhealthy sleep form, how does this affect the body, and how can healthy sleep be cultivated?

Circadian clock disruption by various external factors (zeitgebers) can cause certain disease states and lead to an unhealthy lifestyle (Figure 4). Here it shows how light, food, and exercise can impact the different organ systems and cause issues such as sleep disorders, mood disorders, hypertension, obesity, diabetes, autoimmune disorders, cancer, infertility, and more

(Patke et al., 2020). There are various ways in which circadian clock disruption can cause diseases, cancer, and mental disorders through genes, sleep, and the environment.

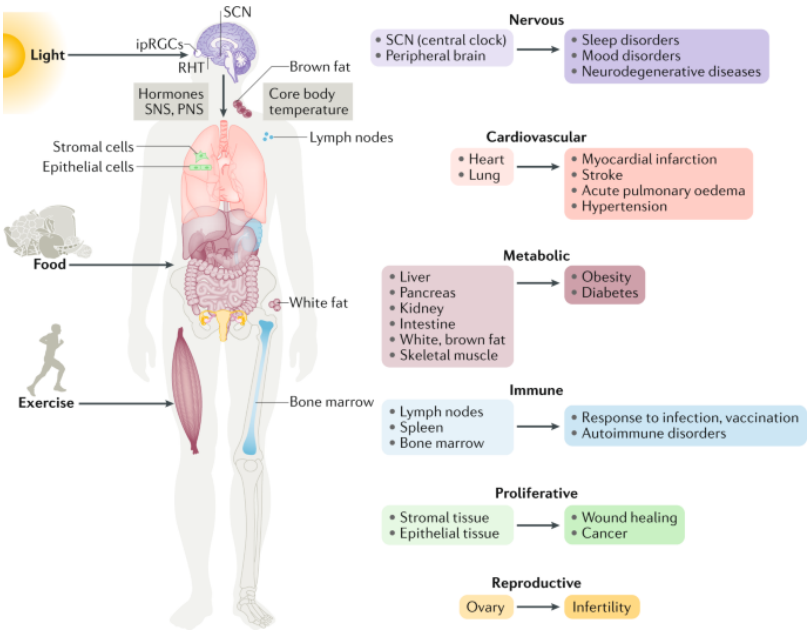

Figure 4. Stimuli affecting systems of the body. Different stimuli (light, food, exercise) affect the different organ systems, processes, and disease states via the SCN (suprachiasmatic nuclei). Patke, A., Young, M. W., & Axelrod, S. (2020). Molecular mechanisms and physiological importance of circadian rhythms. *Nature reviews. Molecular cell biology*, *21*(2), 67–84. https://doi-org.dml.regis.edu/10.1038/s41580-019-0179-2

A dysregulated circadian clock has been linked to many diseases. These include obesity, diabetes, dyslipidemia, neuro-immune disorders, hypertension, and hyperglycemia (Asher & Sassone-Corsi, 2015; Guan & Lazar, 2021; Morris, 2018; Jagannath et al., 2017). These diseases are affected by the circadian clock in a couple different ways depending on type and quality of sleep. For instance, shorter sleep duration has been associated with obesity and diabetes (Asher & Sassone-Corsi, 2015). This is due to the fact that the circadian rhythm influences the endocrine system's ability to regulate insulin resistance and metabolism leading to risks for obesity and diabetes (Reinke & Asher, 2019). Additionally, this sleep duration affects regulating

oxidative phosphorylation and glycolysis that are linked to the development and progression of neuro-immune disorders such as chronic fatigue syndrome (CFS) and multiple sclerosis (MS), which are accompanied by significant sleep abnormalities (Morris, 2018). The second way the circadian clock can alter disease states is through clock genes as introduced in Table 1. Polymorphisms in clock genes (especially BMAL 1) are associated with higher risk of obesity, hypertension, and type 2 diabetes (Jagannath et al., 2017). Additionally, polymorphisms in PER2 and NPAS2 have been linked to hyperglycemia and hypertension respectively (Jagannath et al., 2017). Finally, lifestyle choices such as mealtime and night- versus day-shift work schedules can have a large impact on disease states. Eating meals later in the evening can increase risk for developing obesity and diabetes (Asher & Sassone-Corsi, 2015), as well as working the night shift that can cause dyslipidemia (increased glucose and insulin levels) (Guan & Lazar, 2021). Essentially, disrupting the circadian clock alters genes, hormones, and signaling which in turn leads to disease states, including cancer.

Cancer is one of humans' most feared diseases because of its commonality and lethality and it can be influenced by many external and internal factors, especially those surrounding the circadian clock. Clock genes and the circadian clock disruptions (light exposure, jet lag, sleep disruptions) both increase the risk of cancer risk. Clock genes control and influence many pathways that regulate DNA damage and repair, which is why they are able to increase cancer susceptibility since cancer develops through mutations in damaged DNA (Benna et al., 2017). The four most common cancer related clock genes are NPAS2, CRY2, PER3, and CLOCK, and mutations in these are associated with breast cancer, prostate cancer, and non-Hodgkin lymphoma (Benna et al., 2017). To give an example, clock genes are more prevalent in circulating cancers such as non-Hodgkin lymphoma because without proper circulation through

lymph or blood (which is influenced by clock genes) there can be issues with extra cell proliferation and the formation of neoplastic cells (Gery & Koeffler, 2010). Additionally, clock genes can be repressed by the MYC oncoprotein leading to promotion of cancer (Masri & Sassone-Corsi, 2018). Equally important are the environmental factors that affect the circadian clock which in turn affect cancer risk. Circadian disruption has been classified as a carcinogen and is a risk factor for developing cancer (Shafi & Knudsen, 2019). Exposure to light at night, late-eaters (after 9:30 p.m.), jet lag, shiftwork, and sleep disruption all increase cancer risk, including breast, prostate, lung, ovary, pancreas, colon, and liver cancer (Masri & Sassone-Corsi, 2018; Shafi & Knudsen, 2019). Furthermore, evidence supports this by the following two facts: loss of circadian control is related to less response to cancer treatments and earlier mortality rates, and visually impaired people who are insensitive to light in their environment have a lower cancer risk because these facts show how important maintaining a proper circadian rhythm is for good health and longevity (Shafi & Knudsen, 2019).

Finally, mental disorders and sleep influence each other. The complexity and overlap between the circadian clock, sleep, and mental disorders is difficult to categorize (Gillett et al., 2021). Factors that influence the relationship between them include timing, quality, and duration of sleep as well as behavioral and physiological patterns and conditions, such as those involved in bipolar disorder, ADHD, depression, and BPD (Gillett et al., 2021). Because of these complexities, sleep disruption can result from social reasons, health reasons, or mutations in genes, and the combination of these can lead to a range of sleep disorders (Jagannath et al., 2017). These complexities make trying to “fix” the circadian rhythm of someone with a mental disorder extremely difficult because there are many variables at play. Additionally, these circadian clock abnormalities increase risk of mood disorders, while mood disorders can also

increase circadian clock abnormalities creating a vicious cycle (Landgraf et al., 2016). A specific example of this, as discussed above, would be that night-shift work can lead to circadian clock dysfunction that can increase the risk of depression, which in turn can lead to more issues with the circadian clock and so on (Landgraf et al., 2016). From personal experience, my freshman year of college I worked the night desk in my dorm building. This means between work and my 8:30 a.m. Biology class I slept for about four hours a night! I could definitely tell it took a toll on my mood and ability to control my emotions. Combined with homesickness and my FOMO (fear of missing out), my social and work schedule led to a rather emotional freshman year.

Using all the information we know about how unhealthy sleep habits form, there is a way to use this knowledge to cultivate healthy sleep and hopefully avoid the consequences of circadian clock disruptions. A list of the ways to do this includes increasing duration of uninterrupted sleep, increasing total time of sleep, reducing night work, not eating late in the evening, having regular sleep schedule that does not change, and managing mental disorders with a medical professional so exacerbation of sleep disturbances does not occur. Of course, seeing a medical professional who specializes in sleep, or a sleep psychologist, and discussing sleep with them is always a good idea, too. I believe that this information is very important to everyone, but especially those with mental disorders since they could benefit from this knowledge the most.

Chapter 2: Borderline Personality Disorder

Section 1: The symptomology of BPD

Now that the groundwork of sleep and the circadian rhythm has been laid out, I want to talk about borderline personality disorder (BPD) and then relate it to sleep disorders. The epidemiology of BPD, a type of personality disorder, has been studied and the statistics are shown below. A personality disorder manifests in extreme personality traits that can vary throughout each person and from day to day (Ekselius, 2018). Additionally, personality disorders can interrupt life in various ways that lead to suffering and limitations on daily functions (Ekselius, 2018). The prevalence of personality disorders worldwide is estimated to be 6.1% of people (Marceau et al., 2018). In particular, the prevalence of BPD is estimated to be between 1.6%-5.9% in the United States ("Personality Disorders", 2013). Additionally, BPD predominantly affects women (75% of cases), and it decreases in prevalence in older age groups ("Personality Disorders", 2013). However, there is some doubt on the statistical truth in this number. This could be due to the fact that women are more likely to seek out mental health care than men, and that men are more likely to be diagnosed with depression or PTSD instead of BPD (McLean, 2022). Finally, when considering the genetic components of BPD, it has been associated with between 40-60% heritability (Marceau et al., 2018). A final important statistic to bring up is the suicide rate. This is very important to include because of how high it is. In fact, about 70% of people diagnosed with BPD will attempt suicide at least once in their life and approximately 10% will actually complete this act (*NYP-bpd,* n.d.). This is an abhorrent statistic because the suicide rate is higher for BPD than any other psychiatric disorder (*NYP-bpd,* n.d.).

According to the Diagnostic and Statistical Manual of Mental Disorders, to diagnose someone with BPD they have to have five out of the nine symptoms listed below:

- Efforts to avoid abandonment (real or imagined).
- Unstable interpersonal relationships that follow a pattern of alternating between idealization and devaluation.
- Persistent identity disturbances that involve unstable self-image or sense of self.
- At least two areas of impulsivity that can by self-damaging such as spending, substance abuse, reckless driving, sex, binge eating, etc.
- Suicidal behavior or threats as well as self-mutilating behavior (parasuicidality).
- Instability in mood due to reactivity of mood such as anxiety, irritability, or intense dysphoria that can last anywhere from a few hours to a few days.
- A feeling of chronic emptiness.
- Intensity and difficulty in controlling anger. Can be displayed as a temper, constant anger, or recurrent physical fights.
- Stress-related paranoia or dissociative symptoms ("Personality Disorders", 2013).

These are just a list of symptoms to help identify when a person has BPD, but not every person has all of these symptoms. To further explain a few of these categories, mood instability is defined as, "rapid oscillations of intense affect, with a difficulty in regulating these oscillations or their behavioral consequences," and impulsivity is defined as, "a predisposition to have rapid and unplanned reactions to internal and external stimuli without regard to the negative consequences of these reactions to individuals and others," (Gillett et al., 2021, p. 66). While these are the mental symptoms of BPD, there are physical and biochemical symptoms as well.

From what I have seen with my family member I can confirm that the symptoms above are a true description and that I am intimately familiar with the signs of impulsivity, mood swings, identity issues, fear of abandonment, self-harm, anxiety, and relational issues. However all of these symptoms seem unwelcome and unfavorable, I have also witnessed how some parts of BPD can actually be utilized for good. Many people, including myself, think of the word "disorder" and only think of all the bad symptoms, the mere reasons that make living with a disorder difficult. Despite this, there are good aspects of having BPD according to my family member. This initially surprised me, but on second thought I believe that it makes a lot of sense

to find the good in a situation. Hence, this is why I think it is important to shed a new light on mental disorders: to show that there is a beauty to them even in the pain.

A person with BPD has more intense emotions than their normal counterparts; this can be a good thing because one can feel the good emotions more (McLean, 2022). What makes some people feel content can make those with BPD feel overjoyed. What makes some people feel happy can make those with BPD feel ecstatic. This also means that they feel the bad emotions more strongly than most as well. My family member has told me that however it is hard, it is a great inspiration for their creative side. Having strong emotions helps inspire artwork and songs which has and will continue to allow people to express themselves and to reach others in ways that might not have been possible without the intense feelings. Additionally, the issue with impulsivity can have very intense consequences, but it can also allow people with BPD to be more courageous than they would be otherwise.

Not only does BPD have effects on the symptoms listed above, but it also affects the rest of the body. First, people with BPD have an overall higher heart rate at baseline and during emotional stress than healthy counterparts (Eddie et al., 2018). This suggests that there is an overall increased sympathetic and parasympathetic response (Eddie et al., 2018). Secondly, when BPD causes hormone levels to increase, especially the stress hormone cortisol, there is a significant influence on the brain's structure and function (Marceau et al., 2018). This is important to consider especially because those with BPD have many alterations in their physiological stress reactivity (cortisol involved) compared to healthy controls (Aleknaviciute et al., 2016). This means that the hormones and their paths can be altered from the baseline. To expand a little on this topic, cortisol is a glucocorticoid hormone that is released during social and psychological stress (Adam et al., 2017). Cortisol responds to stress in the short-term (acute)

as well as in the long-term (chronic) (Adam et al., 2017). Cortisol is necessary for the body and brain to do many activities such as energy and metabolic processes, immune system functions, and arousal (Adam et al., 2017). However cortisol is necessary there can be too much of a good thing. Chronically high levels of cortisol can lead to issues with endocrine, nervous, cardiovascular, and immune systems (Lee et al., 2015). Knowing this it is easy to see why people with BPD are more likely to suffer from arthritis, gastrointestinal disease, chronic pain syndromes, hypertension, obesity, diabetes, and many other diseases than their healthy counterparts (Castle, 2019). There are many additional reasons why this could be the case and not everything is known about the specifics behind the increase in disease states for these individuals. These statistics mentioned above are evidence that people with BPD need more specialized treatment plans that address more than just their mental BPD symptoms.

Section 2: How BPD and sleep disturbances affect one another in a vicious cycle, as well as exacerbate unhealthy symptoms of BPD.

Researchers have hypothesized about the relationship between sleep, circadian rhythm disturbance, and psychiatric disorders for years. Only recently is it becoming more and more clear as new research is published (Gillett et al., 2021; Jagannath et al., 2017). In fact, the circadian clock and mental illness form a bidirectional feedback loop in which issues in one area exacerbate issues in the other (Jagannath et al., 2017). Knowing this, it is important to keep the circadian rhythm balanced in order to effectively treat BPD. The most common areas of sleep disruption in BPD involve short sleep duration, short REM sleep, frequent awakening, low sleep quality, long REM sleep duration, and increased sleep latency (Hafizi, 2013). Issues with sleep in individuals with BPD could be due to a general impairment in self-regulation in the body

(Winsper et al., 2017). The idea of "emotional cascades" (dysregulation during the day leads to dysregulation during the night which impacts sleep) supports this theory (Winsper et al., 2017). This manifests biologically in the amygdala and leads to hyperactivity in the limbic system, the emotional and behavior section of the brain respectively (Winsper et al., 2017). Basically, this research is suggesting that since BPD has altered hormonal pathways it could likely alter circadian rhythm. To highlight the point more clearly, individuals without mental disorders are more likely to develop one if they have an altered sleep rhythm due to shiftwork, jetlag, and other issues (Landgraf et al., 2014). Additionally, there is a link between mental disorders (including personality disorders such as BPD) and clock genes (Fleischer et al., 2012). For instance, the clock genes CLOCK/BMAL 1 regulates the production of a precursor molecule for hormones that are very important in mental disorders such as epinephrine, norepinephrine, and dopamine (Landgraf et al., 2014). Not only is dopamine an important hormone in mental disorders, but it is also an important hormone to sleep. Dopamine acts as a key signaling molecule in the regulation of sleep versus wake cycles (Ashton & Jagannath, 2020). However, not much is known, more needs to be researched in the future to address this linkage.

So how does sleep affect the mental symptoms of BPD? In a study done on undergraduates, sleep duration was negatively associated with impulsivity that leads to an increase in risky behavior (Gillett et al., 2021). Additionally, mood instability and sleep patterns were associated in psychiatric populations more than the control populations leading to the idea that sleep dysfunction may be part of the pathogenesis of these disorders (Gillett et al., 2021). In other words, issues with sleep could lead to someone being diagnosed with BPD in the first place. Not only can sleep impact mood and impulsivity of those with BPD, but it can also affect self-injuring and suicidal behaviors (Fitzpatrick et al., 2021).

Another study performed on a randomly selected group of 40 people with BPD experimented with the total sleep time (TST) compared to non-suicidal self-injury (NSSI) behavior (Fitzpatrick et al., 2021). Researchers discovered that the higher the TST the lower the NSSI urges and the lower the overall suicide urge (Fitzpatrick et al., 2021). This is highly important data when thinking about how sleep affects those with BPD. They did find that increasing the TST in people who already had a relatively high TST had a greater decline in NSSI behavior compared to those who have a relatively low TST to begin with (Fitzpatrick et al., 2021). This may be due to the fact that having a higher TST to start leads to less severe symptomology (Fitzpatrick et al., 2021). Additionally, for those who have a low TST, situations that provoke an emotional response have a greater chance of having NSSI and suicide urges rise in order to cope (Fitzpatrick et al., 2021). These are some studies that show just how damaging sleep disorders can be, especially to those who are suffering from mental illness (Fitzpatrick et al., 2021; Gillett et al., 2021). It is clear that sleep disturbances negatively impact mental illness in general, but how do sleep disturbances affect BPD specifically?

Plante et al. (2013), performed a study on how sleep disturbances affect recovery in those with BPD. The recovery from BPD was defined as having a remission of symptoms and a score of over 61 on the global assessment of function (GAF) which offers insight into how well a person is functioning and engaging in meaningful relationships (Plante et al., 2013). This study involved 223 patients with BPD (Plante et al., 2013). Each participant completed the Pittsburgh Sleep Quality Index (PSQI), with a higher score meaning a greater sleep disturbance and then 16 years later they completed it again (Plante et al., 2013). 87% of the surviving patients completed the PSQI (13 died from suicide and 13 died from other causes) (Plante et al., 2013). The results show that there is a significant difference between the PSQI scores of the non-recovered (11.06)

and recovered (8.28) BPD patients meaning that recovering from BPD has a positive impact on sleep (Plante et al., 2013). These results also suggest that having regular sleep disturbances could be a contributing to chronic BPD (Plante et al., 2013). This just further shows that sleep disorders and BPD negatively affect each other in major ways.

Additionally, my family member has personal experience with having issues with sleep disturbances. I have come to find out that on average they sleep for about 5 hours a night. This lack of sleep caused this person to feel more anxious, more emotional, and end up feeling like sleeping is a waste of productivity. Additionally, my family member once went three days without sleep. They cannot think of a trigger for this event, but during this time their BPD symptoms worsened. They had very rapid mood shifts from enormous highs to devastating lows. During these days they were in a manic state where they felt very tired during the day, but at night full of energy. They were more emotional and anxious than usual, bordering on paranoia. As one would assume this lack of sleep was very challenging to day to day life. Some other effects of this lack of sleep were that they hardly ate since their appetite was thrown off and they had extreme memory issues to the point where they did not remember what they learned in class and watched half a season of a tv show and did not remember any of it. Additionally, they began to have microsleeps where they would close their eyes in class or in the dorm and sleep for a short period of time. Eventually, on the fourth day following the third night without sleep they were playing guitar on the couch and fell asleep into a deep nap. It took them awhile to get back to their “normal” sleep schedule, but eventually they did. This is just one of the many stories that people with BPD and sleep disturbances have in which their lives can be thrown off seemingly for no reason.

Because of the connection between sleep and BPD, improvement in BPD symptoms is associated with better sleep quality and vice versa (Hafizi, 2013). Since this is the case, it is important to treat BPD properly and specifically for each patient with special attention being put on sleep and the circadian rhythm. This is especially important because people who have BPD and suffer from sleep problems have a higher risk of suicidal attempts and ideation (Hafizi, 2013). Because of this, along with the host of other reasons, it is imperative that health professionals pay attention to sleep difficulties in their patients (Winsper et al., 2017). Hopefully by first acknowledging and watching for this connection, better care can be given to these patients.

Chapter 3: Treatment

Section 1: Current treatment methods for BPD in a clinical setting.

Psychotherapy

There are a few treatments for those with BPD as of now. Currently, psychotherapy is the most effective, evidence-based treatment for those with BPD (Marceau et al., 2018). One of the biggest issues with psychotherapy is that approximately one-third of the patients do not have a significant response to the treatment (Marceau et al., 2018). This problem could be due to the fact that there is a significant lack of knowledge about the process of matching certain treatments to particular patients in order to have better treatment outcomes (Marceau et al., 2018). The main five types of psychotherapy used for those with BPD, along with their desired outcome and efficacy, are listed below in Table 2.

Table 2: Information on types of therapy used to treat BPD. A list of the most popular therapies used to treat BPD including dialectic behavior therapy, mindfulness-based cognitive therapy, mentalization-based treatment, and transference-focused psychotherapy. Many of these are compared against treatment as usual (TAU) which refers to the use of medication or different types of therapy that are different that the four mentioned above. Additionally, there is a description, desired outcomes, and efficacy of each treatment (Sachse et al., 2011; Stoffers et al., 2012).

Therapy Type	Description	Desired Outcome	Efficacy
Dialectic Behavior Therapy (DBT)	Extensive treatment package that includes sections on emotional regulation, distress tolerance, and interpersonal effectiveness. (Sachse et al., 2011).	To change the patient's ability to handle difficult emotions and behaviors by focusing on mindfulness, interpersonal behavior, emotion regulation, stress tolerance, and improving skills.	Significant improvement of BPD symptoms including anger, suicidal behavior, depression, anxiety, and overall mental health (Stoffers et al., 2012).
Mindfulness-based Cognitive Therapy (MBCT)	Education and experience in mindfulness sessions where patients learn	To improve the patient's attention control, ability to counteract experiential	Improvement was observed significantly in experiential avoidance and retention/attendance

	about thoughts, feelings, meditation, and bodily sensations.	avoidance, and mindfulness practice.	rates. Possible improvement (not significant) in anxiety, dissociation, depressive symptoms, and impulsivity (Sachse et al., 2011).
Mentalization-based Treatment (MBT)	Psychoanalytically-based psychological intervention.	To increase the capacity for reflection and mentalization of the patient, to help the patient understand how their actions affect other people's emotions, and to understand their own emotions and feelings.	Significant positive benefits in reducing suicidality, parasuicidality, interpersonal problems, depression, reduction of overall symptoms, and overall functioning (Stoffers et al., 2012)
Transference-focused psychotherapy (TFP)	A type of psychotherapy in which primitive object relations are transformed into advanced ones.	To integrate representations of the patient's self and others, fix identity diffusion, and modify primitive defenses (Stoffers et al., 2012).	Positive, significant benefits for reduction of BPD severity and treatment retention (Stoffers et al., 2012).

There are a few different therapy options for those with BPD. Each of these have a goal of easing BPD symptoms with verbal communication and either emphasize relationships or focus on acquiring new experiences and skills (Stoffers et al., 2012). One of most well-researched treatments for BPD is Dialectic Behavior Therapy (DBT) and one of the most commonly used to treat BPD (Sachse et al., 2011). DBT is a therapy that incorporates an extensive treatment package that includes sections on emotional regulation, distress tolerance, and interpersonal effectiveness (Sachse et al., 2011), and is very useful for treating BPD. The desired outcome of DBT is to change the behavior of the patient with BPD as well as adapt their ability to contain difficult emotions and feelings by changing the focus (Stoffers et al., 2012). The focus is usually directed towards improving skills, emotional regulation, interpersonal behavior, mindfulness, and stress tolerance (Stoffers et al., 2012). By combining five different studies comparing DBT

versus treatment as usual (TAU), the usual medicine and therapy given by professionals, it was found that DBT has significant benefits to patients with BPD (Stoffers et al., 2012). There was a large positive effect on anger, suicidal behavior, depression, and anxiety (Stoffers et al., 2012). Additionally, there were moderate positive effects on parasuicidality (actions of self-mutilation) and overall mental status (Stoffers et al., 2012). There were other positive effects from the DBT treatment such as a decrease in dissociation, impulsivity, and interpersonal problems, but these were not significant (Stoffers et al., 2012). While DBT is one very useful type of therapy there are others that have different paths to attempt to reach the same goal: relief of symptoms for the patient.

Similar to DBT, is Mindfulness-based cognitive therapy (MBCT) which includes cognitive therapy like DBT, but with training in mindfulness (Sachse et al., 2011). MBCT involves education and experience in mindfulness sessions where patients learn about thoughts, feelings, meditation, and bodily sensations (Sachse et al., 2011). The way MBCT works is that patients will develop a new relationship with their own thoughts and emotions in order to develop more positive emotions and more adaptive coping mechanisms (Sachse et al., 2011). However MBCT has not been used to treat BPD, it does have potential applications that could prove useful. For instance, the application of MBCT to patients with a high risk of suicide suggests that this therapy could be helpful for those with BPD (Sachse et al., 2011). One team of researchers tried using MBCT with BPD patients. Sachse et al. (2011) performed a MBCT clinical study on BPD patients and the majority of the participants attended 2/3 sessions which, compared to the drop-out rates of other therapy programs, is a great rate of retention. The results of this study showed significant improvement in experiential avoidance and retention rates (Sachse et al., 2011). Additionally, the study showed an upward trend in improvement (not

significant) in attention control, dissociation, depressive symptoms, impulsivity, and mindfulness practices (Sachse et al., 2011). There is also the possibility that if anxious symptoms were treated prior to the MBCT sessions, the positive outcomes could be enhanced (Sachse et al., 2011). This is important research towards treating those with BPD. More research needs to be done surrounding this topic as well as treatments involving sleep.

Another option for therapy is called the mentalization-based treatment (MBT). MBT is a psychoanalytically-based psychological intervention meant to increase the patient's ability for reflection and mentalization, to help the patient understand how their actions affect other people's emotions, and to understand the patient's own emotions and feelings (Stoffers et al., 2012). MBT has some of the best evidence in terms of efficacy in two trials against control groups (Stoffers et al., 2012). Both trials showed large significant reductions of suicidality, parasuicidality, depression, and interpersonal problems (Stoffers et al., 2012). Additionally, there were significant decreases in overall symptoms and an improvement in general functioning (Stoffers et al., 2012). Finally, there were non-significant findings for the reduction of anxiety, but further research is needed (Stoffers et al., 2012).

Transference-focused psychotherapy (TFP) is another option for those with BPD. TFP is a type of psychotherapy alters the ideas of relationships in the patient (Stoffers et al., 2012). This is done by changing primitive object relations (polarized, split) into healthy advanced ones (differentiated, integrated) (Stoffers et al., 2012). The goal of TFP is to combine representations of the patient's self and others, resolve identity diffusion, and change the primitive defenses of the patient (Stoffers et al., 2012). In one study, TFP was tested against a control therapy group for 12 months (Stoffers et al., 2012). TFP was found to lessen BPD severity and increase treatment retention significantly (Stoffers et al., 2012). Interestingly, TFP had a few non-

significant negative effects on the patients such as increase in parasuicidality, anxiety, overall general function, and depression (Stoffers et al., 2012). However, these negative findings were all insignificant and this was only in one study (Stoffers et al., 2012). More studies need to be done on BPD patients and TFP treatment in order to determine the efficacy.

Drugs

Another treatment option that differs from psychotherapy is called pharmacotherapy, treating a disorder with a drug. Pharmacotherapy could be appropriate to treat comorbid conditions, but it is not recommended as a primary treatment for BPD (Marceau et al., 2018). Since sleep disturbances are considered a comorbid condition, they could be a potential candidate for treatment of BPD with pharmacotherapy as the biotechnology progresses. The details of the different types of drugs prescribed to those with BPD are listed in Table 3. This information was gathered from one study in which 141 psychiatrists answered questions about their treatment habits with their patients with BPD concerning antidepressants (ADs), mood stabilizers, benzodiazepines, and antipsychotics (APs) (Knappich et al., 2014). ADs are a type of medication to treat depression, APs are medications used to treat psychosis which is a loss of contact with the reality around you, mood stabilizers are used to treat mood changes affiliated with mental disorders, and benzodiazepines (a type of anti-anxiety medication) are used to treat generalized anxiety disorder and reduce panic attacks and extreme worry (National Institute of Mental Health, 2022).

Table 3: Common drugs used to treat BPD. The most common drug types, prevalence of their use in the clinic, and specific examples of each type along with percentages of prescription (Knappich et al., 2014)

Drug	Prevalence	Common Drugs
Anti-depressants (ADs)	98.5% of psychiatrists usually prescribe Ads.	Citalopram and escitalopram (58.6%) are the most common prescribed drugs.
Mood stabilizers	74.6% of psychiatrists usually prescribe mood stabilizers.	Valproate (59.6%), lamotrigine (40.4%), lithium (22.3%), and carbamazepine (20.2%) are the most common prescribed drugs.
Benzodiazepines	71.4% of psychiatrists prescribe benzodiazepines.	Lorazepam (60%) and lormetazepam (16%) are the most common prescribed drugs.
Antipsychotics (AP)	90.6% of psychiatrists prescribe APs.	Quetiapine (70.1%) and olanzapine (18.7%) are the most common prescribed drugs.

The results of this study show that psychiatrists are not comfortable choosing only psychological treatment over medication since the patterns of prescriptions versus psychological treatment show a stronger emphasis on medication (Knappich et al., 2014), demonstrating that pharmaceutical drugs are very critical to the treatment process of BPD. Additionally, it seems that psychiatrists tend to follow a similar pattern of drug prescription (Knappich et al., 2014). To explain, the order of prescription usually went ADs, APs, mood stabilizers, and then finally benzodiazepines (Knappich et al., 2014). This seems like a positive since most psychiatrists follow the same treatment, but it is not always true. Psychiatrists in different areas prescribe different drugs and in different patterns (Knappich et al., 2014). For instance, in other studies, such as one in Britain, the psychiatrists mentioned clozapine as a drug for BPD treatment, but this drug was not even mentioned in the study at hand. The differences in medication prescription patterns are especially evident since psychiatrists in different areas prescribe different medications (Knappich et al., 2014). One possible explanation for the contrast between these psychiatrists is that the research into these drugs and their effects on BPD is not complete. Most psychiatrists agree and say that psychotherapy is more helpful than medicine, but since there is a lack of treatment options, drugs have to fill in the gaps to help people with BPD cope

with their symptoms (Knappich et al., 2014). This shocking discovery alone is enough to warrant the need for more research looking into treatment methods for those with BPD.

Non-traditional Medications

Not much research has been done on the possible benefits of using non-traditional treatments such as cannabis (marijuana) and psychedelics for BPD, but these methods are talked about heavily in media. In my own life I have seen articles, documentaries, and even heard people talk about how these treatments could be the cure we are missing. Below in Table 4 both cannabis and psychedelics are discussed in regard to dosage, efficacy, and possible side effects.

Table 4: Non-traditional drugs for potential use to treat BPD. Shows the regimen, efficacy, and side effects of two different types of non-traditional drugs: cannabis and psychedelics. Cannabis has been shown to not be affective at treating mental disorders, while psychedelics show promising results in the few trials published (Kuypers, 2020; Lowe et al., 2018).

Drug	Dosage/Regimen	Efficacy	Side Effects
Cannabis/Marijuana (Lowe et al., 2018)	Usually, self-medicated (dose unknown). In a study of 1,429 people from 18 different countries people report that the use cannabis medically for pain, anxiety, and depression. People claim use it for sleep related issues as well.	Use of marijuana for "self-medicating" is actually more harmful than therapeutic	Cannabis use can increase the risk of being diagnosed with a mental disorder and has been shown to exacerbate symptoms including feelings of anxiety and suicide risk. There are also physical risks such as impaired cognition, memory, coordination, and judgment. Also, other physical risks include addiction, progression to illicit drugs, and bronchitis and other chronic lung issues from smoking.
Psychedelics (Kuypers, 2020)	LSD: 10-20mcg with a three day cycle (1 day "on" and 2 days "off")	Full psychedelic dose as well as lower dose (no psychedelic	During days of dosing participants reported feeling physical discomfort (such as mild headaches) and

	Psilocybin: <1-3mg	experience) both show promising results in trials with participants having increased cognition and less depressive symptoms.	increased anxiety. Additionally, participants must be weaned off of other medication such as anti-depressants which can cause increased risks that may outweigh the benefit.

Cannabis (marijuana) has traditionally been illegal in many states, but there is a new tide turning of legalized medical use and recreational use of cannabis. This legalization has occurred because of increased use, decreased perceived risk, and an increase in general acceptance in the public (Lowe et al., 2018). Cannabis comes from the *Cannabis sativa* plant and contains cannabinoids such as delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) (Lowe et al., 2018). Both of these cannabinoids affect the body, but the primary psychoactive "high" part of cannabis use comes from THC (Lowe et al., 2018). Cannabis use disorder (CUD) is much higher in those with mental illness, like personality disorders such as BPD (Lowe et al., 2018). People who self-medicate with cannabis as a way to treat mental disorders say that the perceived benefits include symptom relief from schizophrenia, major depressive disorder (MDD), bipolar disorder, anxiety, panic attacks, and post-traumatic stress disorder (Lowe et al., 2018). For instance, in a study across 1,429 people from 18 countries the individuals who reported that they self-medicate with cannabis gave pain, anxiety, and depression as the top three reasons for using (Lowe et al., 2018). Other studies have also found that lack of sleep or poor sleep quality is another major contributor to the reasons why people begin to self-medicate (Lowe et al., 2018). This makes sense since we have previously discussed how mental illness tends to come with sleep disturbances as well.

The prevalence of self-medication with cannabis is concerning when considering that many studies have found that cannabis use actually has more harmful effects than therapeutic

ones (Lowe et al., 2018). For instance, one study spanning 40 years with about 400 individuals found that cannabis use is positively correlated with a MDD diagnosis (Lowe et al., 2018). Additionally, cannabis use has also been shown to increase depressive symptoms (Lowe et al., 2018). While these data are not on BPD, it can be assumed that it would have similar effects especially since depression is a major symptoms of BPD. Other reasons why cannabis use could be harmful are physical. Cannabis use causes impaired short-term memory, motor control, and judgement (Lowe et al., 2018). Additionally, cannabis can cause THC-induced paranoia and psychosis (Lowe et al., 2018). Some of the biggest physical harms that cannabis can cause are addiction, sleep problems, lung inflammation (from smoking), and progression to more intense and deadly drugs (Lowe et al., 2018). It seems from this study that cannabis is not a good option for treating BPD and sleep disturbances because of the strong risks versus the perceived benefits. However, this is only one article and few other studies on BPD and cannabis have been done. Basically, what I am saying is that this article could have some personal bias. When thinking of other similar disorders such as insomnia, anxiety, and depression cannabis seems to have a positive effect. Kuhathasan et al. (2022) performed a study exploring cannabis use as a way to treat insomnia related to depression and anxiety. They found that people who had insomnia due to their anxiety or depression and used cannabis had significant improvement of symptoms (Kuhathasan et al., 2022). These conflicting articles show that cannabis in regards to mental disorders, especially BPD, needs to be studied more in depth to uncover the nuances to using cannabis as a treatment.

Psychedelics, such as Lysergic acid diethylamide (LSD) and psilocybin, could be a much better treatment for BPD than cannabis and have real beneficial results in many studies (Kuypers, 2020). These psychedelics are usually used to cause mind-altering effects and

distortions of the world around the user (Kuypers, 2020). They also are able to increase emotional empathy, mood, social behavior, and reduce negative emotions such as stress, fear, and sadness (Kuypers, 2020). Microdosing is the process of taking much less than the usual amount to stimulate the psychedelic affects, but still having the positive affects listed above (Kuypers, 2020). Preliminary studies have shown that psychedelics can treat depression symptoms and have cognitive benefits, but not enough is known about them in regard to mental health let alone BPD (Kuypers, 2020). Microdosing psychedelics needs to be researched more in the future especially in groups of individuals with BPD.

Circadian Medicine and Sleep Medication

Many medical practitioners are advocating for a safer and lower-cost intervention strategy for many pathologies including mental disorders that are comorbid with sleep disturbances; this new type of treatment is called circadian medicine (Patke et al., 2020). This is a very important upcoming field of study since treatments such as these positively affect the relief of symptoms of depression and mood behaviors (Albrecht, 2020). Some of the different types of circadian medicine along with their efficacy are listed below in Table 5.

Table 5: Information on types of circadian medicine. The three different types of circadian medicine (chrono-phototherapy, chrono-diet, and chrono-exercise) along with their descriptions, regimens, and efficacy (Lee et al., 2021).

Types of Circadian Medicine	Description	Regimen	Efficacy
Chrono-Phototherapy	Exposure to light at certain times of the day.	Using bright light therapy from light devices or natural morning light.	Can improve mood, alleviate symptoms of depression and anxiety, regulate melatonin, and help regulate sleep/wake alternations. Also,

			can help with disease prevention.
Chrono-Diet	Restricting food intake to only certain times of the day.	Limits food to a certain window with fasting in between. Common examples are 8 hrs of food with 16 hrs fasting or 6 hrs of food with 18 hrs of fasting.	Can help with disease prevention and impact on physiology.
Chrono-Exercise	Scheduling exercise for certain times of the day.	Exercising in the morning or at night depending on risk factors and what chronotype you are (morning or night person).	Can counteract environmental and genetic reasons for circadian rhythm disruptions.

The three types of circadian medicine that are prevalent for discussion are chrono-phototherapy, chrono-diet, and chrono-exercise (Lee et al., 2021). First, chrono-phototherapy is the exposure to light at certain times of the day whether this is natural lighting or light from a therapy light device (Lee et al., 2021). The use of chrono-phototherapy has been shown to help alleviate symptoms of depression and anxiety, regulate melatonin levels, improve mood, help regulate sleep, and aid in disease prevention (Lee et al., 2021). Most studies focus on morning bright light exposure or daytime blue light exposure (Lee et al., 2021). Chrono-phototherapy could have a positive effect on those with BPD and sleep disorders by realigning their circadian rhythm and decreasing the cycle of worsening BPD symptoms via exacerbating sleep disturbances. Second, chrono-diet is eating at certain times in order to match the eating habits wakefulness part of the circadian rhythm (Lee et al., 2021). The benefits of chrono-diet include aiding in disease prevention and impacting the overall physiology of the body (Lee et al., 2021). Usually chrono-diets follow the pattern of limiting food intake to a certain number of hours a day and fasting for the rest of the day (Lee et al., 2021). For instance, most studies had patients

follow the pattern of 8 hours of food with 16 hours fasting or 6 hours of food with 18 hours of fasting (Lee et al., 2021). These methods all saw some sort of improvement with sleep wake cycles (Lee et all, 2021). Chrono-diet seems to be less of a viable option for those with BPD and sleep disturbances since more research needs to be conducted to explore this topic. Finally, chrono-exercise consists of scheduling exercise at certain times of the day depending on what chronotype one falls into (Lee et al., 2021). For instance, if you are a morning person versus a night person different times of exercise can affect you differently (Lee et al., 2021). Exercising in the morning or at night comes with different benefits and risks depending on each person (Lee et al., 2021). Chrono-exercise is shown to counteract environmental and genetic reasons for circadian rhythm disruptions such as temperature of room, noise level, levels of fatigue, or sleep disorders (Lee et al., 2021). Chrono-exercise seems to be a great option for those with BPD and sleep disorders since it could potentially decrease symptoms of the sleep disorder, which in turn can reduce symptomology of BPD.

Once the technology, pharmacology, and socio-political atmosphere develops further, circadian medicine will be able to personalize treatment plans for all of those suffering from mental disorders (Roenneberg & Merrow, 2016). When I say socio-political atmosphere, I am talking about the way people view mental disorders and sleep disorders. From what I have seen there has been a history (especially in older generations) of disregarding these disorders as not important, foolish, and embarrassing. However it has gotten better since I was younger with more conversation and opportunities for help, there is still a long way to go with mental disorders. Anyway, circadian medicine can be split into behavioral changes as well as drug-related prescriptions. Other ideas for this type of medicine include chronotherapy, light therapy, and circadian intervention (Patke et al., 2020). These types of treatments have shown some

success in people struggling with sleep and circadian rhythm disruption and sleep disorders (Jagannath et al., 2017).

If the above treatments do not work effectively then drugs can also be prescribed (Roenneberg & Merrow, 2016). Usually, drugs that are already on the market that address sleep related issues are used (Roenneberg & Merrow, 2016). However, these are not always effective and potent pharmacological drugs are still lacking (Jagannath et al., 2017). A few of the available sleep medications are discussed in Table 6.

Table 6: Information of types of sleep medication. These medications are over the counter sleep meds, antidepressants with sedating effects, and prescription sleeping pills (Mayo, 2022; Pacheco, 2022).

Types of Sleep Medicine	Common Drugs	Efficacy	Side Effects
Over the Counter Sleep Meds	Melatonin, diphenhydramine, doxylamine, and valerian.	Melatonin – Works to boost natural levels of melatonin for those with sleep-wake phase disorder or shift work disorder but it is not FDA regulated. Diphenhydramine – FDA approved antihistamine (Benadryl) but has been shown to not work effectively. Doxylamine – Has sedative effects and works well but has 31 major drug interactions and should not be taken for long periods of time. FDA approved antihistamine. Valerian - Used to treat insomnia and anxiety, but	Melatonin can cause depression, daytime sleepiness, and headaches. Diphenhydramine can cause dizziness, disturbed coordination, and epigastric pain. Doxylamine can cause drowsiness, dry mouth, and dizziness. Valerian can cause headaches, strange dreams, and cognitive dysfunction (Pacheco, 2022).

		evidence as an effective treatment is inconclusive. Not FDA regulated.	
Antidepressants with Sedating Effects	Amitriptyline, Mirtazapine (Remeron), and Trazodone.	These drugs are not approved by the FDA for sleep related disorders. However they might be prescribed if a sleep disorder is comorbid with anxiety.	Side effects include dizziness, headache, dry mouth, nausea, change in weight, memory issues, bowel issues, and suicidal thoughts.
Prescription Sleeping Pills	Daridorexant, Silenor, Lunesta, Dayvigo, Rozerem, Belsomra, Restoril, Halcion, Sonata, and Ambien.	The drugs can help people fall asleep and stay asleep. However, some of them can lead to dependence.	Side effects include dizziness, headache, bowel issues, drowsiness, allergic reactions, hallucinations, suicidal thoughts, and memory issues (Mayo, 2022).

The three types of medicine for sleep disorders are over-the-counter sleep aids, antidepressants with sedating effects, and prescription sleeping pills (Mayo, 2022; Pacheco, 2022). Over-the-counter sleep medications are those that anyone can buy regardless of diagnosis of a sleep disorder. These over the counter sleep aids include the well-known melatonin as well as diphenhydramine, doxylamine, and valerian (Pacheco, 2022). These vary widely in their efficacy and side effects. Melatonin and valerian are not FDA approved while diphenhydramine and doxylamine are FDA approved as antihistamines (Pacheco, 2022). However diphenhydramine and doxylamine are FDA approved they are not the best option as a sleep aid since they are not proven to be effective, and they have major drug interactions such as aspirin and acetaminophen (Pacheco, 2022). These over-the-counter sleep aids can cause side effects such as dizziness, daytime drowsiness, and headaches (Pacheco, 2022).

If these over the counter sleep aids do not work, there are other options as well. One of these options is antidepressants with sedating effects. Antidepressants are not FDA approved as a

sleep remedy, but they can be prescribed for those with a comorbid mental disorder (Mayo, 2022). These antidepressants with sedating effects include Amitriptyline, Mirtazapine (Remeron), and Trazodone, and have side effects such as dizziness, headache, nausea, memory issues, and suicidal thoughts. (Mayo, 2022). Finally, another option if the over the counter sleeping aids do not work, you are not suffering from a comorbid mental disorder, or they are deemed necessary are prescription sleeping aids. Prescription sleeping aids include Daridorexant, Silenor, Lunesta, Dayvigo, Rozerem, Belsomra, Restoril, Halcion, Sonata, and Ambien (Mayo, 2022). These drugs have been proven to help people fall asleep and stay asleep however these drugs do have side effects such as dependence, dizziness, headache, bowel issues, drowsiness, hallucinations, suicidal thoughts, and memory issues (Mayo, 2022). As can be seen, there are options for medications that aid in sleep, but the side effects and lack of FDA approval can lead to a tricky recovery.

The treatment options that I have discussed thus far are all of the current ways to treat BPD and sleep disorders. It is important to mention before continuing to my suggested holistic treatment for people with BPD and sleep disorders that as of now there is no standard way to treat BPD (Knappich et al., 2014). In fact, few studies have found the common medication group of selective serotonin reuptake inhibitors (SSRI) to be effective (Knappich et al., 2014). Additionally, the guidelines in different countries (such as the UK and the USA) have very different and often opposing treatment strategies which leave clinicians wondering what the best way to treat BPD really is (Knappich et al., 2014). This could be due to the socio-political atmosphere that I mentioned above; since mental disorders, especially BPD, are stigmatized they often go understudied which can lead to discrepancies in how they should be treated. Is this

really all we can do for those with BPD and sleep disorders? Is there any other way to help these people?

Section 2: A more holistic treatment for people with BPD who are also suffering from sleep related issues.

One of the most important things to consider when thinking about treatment for those with BPD, in my opinion, is personalization of the treatment. The health of every single person varies greatly in general and when it comes to mental disorders such as BPD, treatment should be specific to the individual. There are multiple ways to do this either by trial and error, scientific ways to predict treatment outcomes, or by planning with the patient (Marceau et al., 2018). Two of the major ways to predict treatment outcomes are neuroimaging and gene biomarkers (Table 7). There is a shift in the medical field to try and address the issue of non-personalized treatment through utilizing neurobiological markers (genes, neuroimaging, etc.) to enhance individualized treatment and care (Marceau et al., 2018). These markers would be able to predict clinical outcomes of certain treatments and therapies for each patient. A systematic review performed by Marceau et al. (2018) discovered that certain biomarkers can predict the results of psychotherapy outcomes in patients.

Table 7: Ways to predict treatment outcomes in individual patients with BPD. Descriptions, efficacy, and downsides for the two innovative ways, neuroimaging, and genetic biomarkers, to predict how a patient will respond to psychotherapy (Marceau et al., 2018).

Treatment Prediction Methods	Description	Efficacy	Downsides

Neuroimaging	Analyzes brain activity before and after psychotherapy to predict effectiveness of treatment.	Studies on structural and functional neuroimaging show an ability to visually see treatment outcomes, but most studies have very small sample sizes.	A variety of neuroimaging processes and a general lack of research on the topic.
Genetic Biomarkers	Analyzes the methylation patterns of certain genes to predict psychotherapy outcomes.	Some studies show significant results, but others do not.	A general lack of research on the topic (only three studies were identified).

One of these biomarkers is called neuroimaging. Neuroimaging is the process of using specific equipment (such as an MRI) to view areas of the brain and note size, activity, and abnormalities (Marceau et al, 2018). Functional MRI research on the neuroanatomy of those with BPD has mainly focused on five domains: emotion regulation, resting-state, pain sensation, emotion perception, and emotion-cognition interactions (Marceau et al., 2018). Additionally, one study in particular found that there was a decrease in the brain activation of the anterior cingulate and prefrontal regions after psychotherapy (Marceau et al., 2018). These areas have been linked to an emotion regulation capacity in BPD; the results show an increase in emotion regulation capacity (Marceau et al., 2018). This would be especially useful to address the common BPD symptoms of emotion dysregulation and impulsivity (Marceau et al, 2018). With this knowledge, neuroimaging could be used to see if and how psychotherapy is affecting these areas compared to a patient's baseline.

Another biomarker that is able to predict psychotherapy outcomes is genetic biomarkers. When considering biomarkers in genomics, findings indicated that methylation or demethylation of the BDNF gene can be influenced by psychotherapy which directly changes cognition (Marceau et al., 2018). Additionally, the methylation profiles of APBA3 and MCF2 genes are

potential biomarkers that can predict psychotherapy outcomes in specific patients (Marceau et al., 2018). These genes could be used similarly to the neuroimaging to see if psychotherapy is working and how well. These biomarkers as well as others need to be further explored to clarify their role in influencing psychotherapy outcomes (Marceau et al., 2018). This is considered to be a very new and exciting field of study. In fact, researchers interested in this topic are advocating for a multilevel approach to focus on the patient's subjective experience along with both the epigenetic regulation and gene-environment interaction (Marceau et al., 2018). Hopefully this will allow clinicians to have a better idea of their patient's genomic profile and how it can impact treatment with psychotherapy in particular.

Conclusion

Acknowledging all of the above information such as how sleep disorders affect mental disorders, the intense symptomology of BPD, the limited treatment options for BPD, and an ideal holistic view of treatment for those with BPD, it is clear that the research to date is not enough. The treatment options listed above are quite frankly unacceptable since the side effects are intense and the suicide rate is so high. Additionally, a special emphasis needs to be put on treatments for BPD in regard to sleep considering the chronic issues that sleep disorders can cause such as increased risk of disease, cancer, and mental disorders. The treatment options are limited because there is little research done on how these drugs and therapies affect the patients. I believe this is due to the socio-political atmosphere we are in, where mental disorders (especially personality disorders) are not deemed as important as other types of disorders, illnesses, and diseases. More needs to be done for those suffering with BPD and sleep disorders, and more attention needs to be drawn to research, exploration, and personalization of treatment. Hopefully through more investigation into ways to predict treatment outcomes such as neuroimaging and genetic biomarkers, more personalized treatment can be offered to these people. Through a holistic view of a whole person through treatment plans that are specific to each individual (such as circadian medicine and treatment prediction methods), it is possible to alleviate some of the symptoms of BPD and sleep disorders, grant these people back a sense of control and self-autonomy over their lives, and strive towards the possibility of recovery.

In a book titled *Beyond Borderline-True Stories of Recovery from Borderline Personality Disorder*, a conglomerate of twenty-four stories about recovery from BPD highlights how difficult this disorder is and how no way to "recovery" is the same across individuals. While all twenty-four of these stories are different, they all share a common theme of needing a treatment

that works well for them. In this book, the former president of the National Alliance on Mental Illness, Jim Payne, emphasizes how important this is when he states, “These survivors hit their mark in helping to change the conversation about borderline personality disorder (BPD), from one of fear and misunderstanding to one of empathy, evidence-based treatment, and hope. BPD is a relatively new DSM diagnosis with a ten percent suicide rate- and relatively new evidence-based treatments. […] These BPD survivors describe more stable, less chaotic lives, as well as pure gratitude for the mental health professionals who diagnosed their BPD and provided either evidence-based treatment or otherwise compassion and committed care” (Hoffman & Gunderson, 2016, p.i). Basically, Payne is saying that people with BPD are very grateful for evidence-based treatment, compassion, and committed care more than anything else.

I believe that this book and my thesis should serve as a wake-up call to anyone who has a loved one with BPD or who works in a clinical setting with those with BPD, to always act in a committed and ethical way. This book has woken me up to what my family member has gone through at some point or another and how the disorder truly affects people. Hearing the raw, emotional stories of so many who have had BPD has reiterated the importance of finding better treatment and personalizing it to each person. My family member struggles with many different symptoms of BPD, but what they struggle with the most is wanting more control so they can feel like themselves again. Having BPD is an hourly, intense struggle and I believe that having a little more control over their lives through a personalized treatment plan would make a world of difference.

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