Depression: Pathophysiology And Pharmacological Treatments

Investigated Disease Process

Depression rates have risen over the years and it has been considered a debilitating disease for many. Working in the oncology field, I see this manifest in many of the patients I care for on a daily basis. Major depressive disorder is different from having feelings of being down or just sad for a few hours or a couple of days. Depression is also different from grief over losing a loved one or experiencing sadness after a trauma or difficult event. It is not a condition that can be willed or wished away. People who have depression cannot just “pull themselves” out of it or just ignore the symptoms. There is not one know cause of depression, but instead, it is attributed to many biological and external factors.

Major depressive disorders (MDD) that some people suffer from are known as bipolar or unipolar disorders. If this disease is not diagnosed and managed appropriately, it can be considered life threatening. The National Institute of Mental Health (2018) states that this disease also includes a long list of symptoms such as feelings of worthlessness, fatigue, restlessness, difficult sleeping and persistence sadness, as well as suicidal thoughts just to name a few. Impacts of this disease on a person’s family members can include irritability and frustration, with an individual’s consistent feelings of sadness and hopelessness. I choice this disease due to the overwhelming numbers of newly diagnosed middle aged young females suffering from cancer whom are diagnosed on a daily basis.

Pathophysiology

Despite recent advances in neuroscience research, the neurobiological mechanisms underlying the pathophysiology of depression remain poorly understood (Levy, Boulle, Steinbusch, van den Hove, Kenis and Lanfumey, 2018). The development and course of major depressive disorders are likely to be mediated by a complex interaction between genetic and environmental factors which makes it hard for someone to receive an effective therapy and medicinal plan. Having a deeper understanding of the exact molecular, cellular and structural mechanics involved, psychiatrists and therapists can develop a further plan for therapy.

The amygdala is an integral part of the limbic system involving cognitive and emotional processing. This part of the brain is associated with fear and anxiety (LeDoux, 2000). A patient undergoing magnetic resonance imaging (MRI) aids in the diagnosis of the depressed by seeing an increase or decrease of activity of the amygdala. Use of positron emission tomography (PET) imaging can show an increase in the amygdala activation as well as metabolism in MDD patients (Drevets, 2003). Amygdala activity was increased prior to medicating patients, and given that hyperactivity could lead the3 amygdala activity reduction seen in MDD, it is possible that the antidepressants prescribed could in fact decrease the activity as well (Levy et al., 2018)

The hippocampus is also another major part within the limbic system that is known to be vulnerable to stress and other environmental factors as well. This part of the brain is critical to

one’s cognitive process and regulating emotions (Bartsch and Wulff, 2015). When viewing an MRI of the hippocampus, there is a reduction of activity in recurrent depression. When treated with electroconvulsive therapy (ECT) or antidepressants, the depressed person shows an increase hippocampal volume, which shows how crucial this part of the hippocampus plays in depression.

The prefrontal cortex is the next area of the brain that is involved with processing sensory input and motor functions. This plays a major role in regulating the appropriate emotional responses such as anxiety or fear (Ongur and Price, 2000). The prefrontal cortex has also been associated with decision-making, personality expression and social behavior. Neuroimaging studies showed a reduction in size of multiple areas of the prefrontal cortex in people that are diagnosed with MDD (Drevets, 2000). The prefrontal cortex is strongly related to amygdala and the hippocampus and the activity of subdivisions, which has been widely studied in depressed patients. Prefrontal cortex abnormalities that are observed in people with MDD are seen to be partly corrected with antidepressants.

Through continuous research it has also been seen that an over production of the stress hormone known as cortisol was also found in individuals diagnosed with depression. This is all linked to the hippocampus which is the region of the human brain that is involved in making memories and emotions. The overproduction of cortisol has been shown to cause the hippocampus to shrink in size, which can cause a decrease in the hippocampus’ receptors that are used for serotonin. The hormone serotonin functions as a neurotransmitter in the human body and it allows the body to process emotions. Some also believed that a decreased amount of serotonin taken in by the hippocampus due to the decreased receptor sites contributes to an individual becoming depressed.

Chemicals that transmit messages from neuron to neuron within the brain are called neurotransmitters. Monoamines, serotonin and norepinephrine are the known human neurotransmitters and studies show that these neurotransmitters are mostly responsible for controlling mood. One hypothesis is that a deficiency in neurotransmitter monoamines can cause depression, and with the use of medications that increases the level of monoamines depression can be alleviated.

The Permissive Hypothesis states that emotional behavior is controlled by the balance of serotonin and norepinephrine, which in turn results in a balance between serotonin and noradrenalin which ultimately controls mood (Prange, Wilson, and Lynn, 1974). Regulation of mood, sleep and appetite are linked to serotonin, which is also found to be a pain inhibitor. Norepinephrine is shown to cause a raise in the blood pressure by the constricting of blood vessels, and it is also linked to contributing to anxiety. Research by scientists have identified additional neurotransmitters, dopamine, acetylcholine and glutamate all can also play a role in depression (Prange, Wilson, and Lynn, 1974).

Learning and the enhancement of an individual’s brain is linked to the neurotransmitter acetylcholine. A person’s perception of reality, motivation and the brain’s reward system is linked to the neurotransmitter dopamine, and studies show that a decrease level of this neurotransmitter can lead to psychosis. Cognition and learning along with memory are linked to the neurotransmitter glutamate.

Research has found that an individual’s genes can also be linked to depression as well. When

exposed to stress, studies show that variations in an individual's serotonin-transporter gene (5-HTT) can lead to depression. Two copies of this gene are passed down to the individual by the parents, and individuals with only one these serotonin-transporter genes have proven to be more likely to become depressed following a stressful life event. Other variations in the DNA sequence have also been identified as a contributing factor in the development of depression like the G1463A variance (Prange, Wilson, and Lynn, 1974).

Standards of Practice

Depression disorders are very complex and the treatments for these disorders can be a very lengthy process. Studies shows that the treatment of choice for depression is a combination of psychotherapy and antidepressants. Other therapies such as electroconvulsive (ECT) and somatic can also be included within the combination of treatment for depression. Because of the difference of each individual, figuring out a treatment plan that works for the individual is sometimes complicated. Studies show that the assessment for depression should consist of several different components, which includes a history of present and past illness, family history and psychiatric history. Occupational and social history should also be a part of the general assessment for depression. Use and abuse of substances should also be considered when doing an assessment for depression. Collaboration between other health care worker and the patient's psychiatrist should also be included in the patient's plan of care. After the beginning of treatment, close monitoring is imperative in order to notice behavior changes and the response to medication.

Major depressive disorders are diagnosed by Psychiatrists according to criteria that is defined in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV). The patient must experience at least 2 weeks of loss of interest or pleasure in the activities of life, or a depressed mood to meet the criteria of the DSM-IV for major depressive episode or disorder. The DSM-IV list nine symptoms of depression, and the individual my experience at least five of these symptoms and they must cause significant impairment in work, social or other areas of daily functioning (Rosenthal, 2008).

Symptoms

1. Fatigue or loss of energy
2. Insomnia or sleeping to much
3. Depressed mood most of the day
4. Agitation or psychomotor retardation noticed by others
5. Diminished interest or pleasure in all or most activities
6. Feelings of worthlessness or excessive guilt
7. Diminished ability to think or concentrate, or indecisiveness
8. Significant unintentional weight loss or gain
9. Recurrent thoughts of death

Suicide risk and safety assessment should be conducted to assess for suicidal ideation, thoughts and/or plans. This is a guide in the identification of any specific psychiatric symptoms and conditions that may increase the individual's likelihood of acting on suicidal thoughts and ideas. An additional safety assessment to evaluate the potential risk to others should also be included.

Pharmacological Treatments

In Arizona, where I currently reside, antidepressants are the first choice of treatment for individuals who suffer with depression. This medication is standard practice within the local community and often used in combination with psychotherapy. This follows the evidence-based guidelines for the treatment of depression in Maricopa County Department of Mental Health. The patient's characteristics and symptoms are what guides the choice of medication for the patient's treatment.

Selective serotonin reuptake inhibitors (SSRIs) or Serotonin-norepinephrine reuptake inhibitors (SNRIs) are noted as the first-choice medications in my community because they have fewer side effects that any other antidepressants, which makes them safer. Inhibiting presynaptic serotonin reuptake is an action of SSRIs, and inhibiting serotonin and norepinephrine reuptake at higher doses is the action of SNRIs. Weight gain, insomnia, diarrhea, agitation and sexual dysfunction are all side effects of the antidepressant SSRIs, there is also risk of gastrointestinal bleeding. Zoloft, Paxil and Lexapro are all examples of SSRIs. SNRIs' side effects include dry mouth, sweating weight gain and also sexual dysfunction, and Effexor and Cymbalta are examples of this type of antidepressant.

Another type of antidepressant that is used if success is not gained with the use of SSRIs or SNRIs. Norepinephrine-dopamine reuptake inhibitors (NDRIs) is the alternate choice, and an example is Wellbutrin. Wellbutrin works by inhibiting the presynaptic reuptake of norepinephrine and dopamine, its side effects are much similar to the others with dry mouth, nausea and weight gain, but it has not been linked to any type of sexual dysfunctions (Adams, Miller and Zylstra, 2008). The next antidepressant is Remeron and it is known as an atypical antidepressant, it works by enhancing the neurotransmission of norepinephrine and serotonin and by blocking the B-2 adrenergic receptors. This medication is usually prescribed for the individual at night time because of its sedative qualities.

Cyclic antidepressants also known as tetracyclic and tricyclic help depression by blocking the reuptake of the neurotransmitter's norepinephrine and serotonin which in turn making these chemicals have increased availability in the brain (Dold and Kasper, 2008). Other cyclic antidepressants include Imipramine and Amitriptyline, which carries many side effects including seizures, tremors confusion and even irregular heartbeats.

Monoamine Oxidase Inhibitors (MAIOs) are antidepressants that are considered last option antidepressants. These antidepressants are prescribed to individuals that are unsuccessful with all other types of antidepressants. MAIOs works much like all other antidepressant by changing the levels of the human's brain chemicals, and it prevent monoamine oxidase a well-known enzyme from removing neurotransmitters which include dopamine, norepinephrine and serotonin from the brain. Good examples of this antidepressant are Nardil and Marplan, and they are very complication medications. They cannot be taken with foods containing Tyramine which is an amino acid that acts to regulates the human's blood pressure, for the chance of causing the individual's blood pressure to become dangerously high.

MAOIs also cannot be taken with other antidepressants because the combination of the two medications can cause Serotonin Syndrome, due to the excess level of serotonin that is caused by to combination of the two medications (Dold and Kasper, 2008). Once an individual has been

diagnosed with Serotonin Syndrome immediate medical attention is needed for the individual.

The impact of depression and treatment of depression in my community show at that the rates of hospitalization due to metal health reasons for Maricopa County resident consistently lag behind the rates for Arizona from 2009-2016 (Maricopa County Health Assessment, 2017). The analysis of emergency department visits for mental health reasons tell a different story of hospitalization. According to the numbers the emergency department visits for mental health reasons, children and adults have be dramatically higher for Maricopa County residents as a whole, ranging between 45 to slightly more that 100 percent high between 2009-2016 (Maricopa County Health Assessment, 2017). The age-adjusted death rates for suicide in Maricopa County have been consistently higher between 2004-2013, and while rates appear to be leveling off, the rates appear to be demonstrating an increasing trend,