DRUG TREATMENT FOR Schizophrenia

The final assignment for this class will be a 10-page critical review of the drug treatment for a psychiatric disorder (broadly defined to include psychological and neurological disorders as well). The review will use peer-reviewed sources to evaluate the current drug treatment modalities for the selected disorder and determine the adequacy of those treatments. The paper will be evaluated on the inclusion of the following information:

Introduction
Evaluate the disorder in terms of symptomatic and behavioral presentation. Include the time, course, and progression of the disorder. Evaluate and explain special features of the disease epidemiology.

Theory
Evaluate the predominant theory or theories regarding the biological basis of the disorder. Explain the disorder in terms of pertinent neurotransmitter and receptor theories and describe the pertinent evidence of their involvement. Analyze the neurotransmitter systems in terms of the involved receptors and the use receptor agonists and antagonists in the treatment of the disorder receptor. Include information on the anatomic changes to the central nervous system as appropriate to the topic.

Treatment
Evaluate drug therapies for treating the disorder based on the current understanding of the biological basis of the disorder and the corresponding behavioral effects of the disorder. Explain pharmacokinetics and pharmacodynamics in relation to the disorder and corresponding drug treatment. Describe any side effects and adverse effects of the drug treatment and their biological basis, including issues related to contraindications, interactions, drug metabolism, and elimination. In addition, explain risks, benefits, and ethical implications for high-risk and exceptional treatment conditions.

Conclusion
Summarize theories of psychiatric disease as they relate to principles of drug action within the chosen topic. Evaluate advantages and disadvantages of the current theory of the disorder and its treatment and evaluate any controversies regarding ethical and/or risk-benefits perspectives associated with the current treatment. Describe possible areas for future research.

- Must be 10 to 12 double-spaced pages in length (not including title and reference pages) and formatted according to APA style as outlined in the Ashford Writing Center. (Links to an external site.)
- Must include a separate title page with the following:
  - Title of paper
  - Student's name
  - Course name and number
  - Instructor's name
  - Date submitted
- Must use at least five peer-reviewed sources in addition to the course text.
- Must document all sources in APA style as outlined in the Ashford Writing Center.

PLEASE LOOK @ NEXT Pages →

- Must include a separate reference page that is formatted according to APA style as outlined in the Ashford Writing Center.

PLEASE NOTE:
When you are Discussing the Drug treatment For the Disorder, PLEASE DO NOT use Clozapine, COCAINE, OR Cannabis. Choose another one. Also, use the Book Reference (Advokat, Comaty, & Julien, 2018) as a Reference Too.

Topic For Critical Review Paper

Schizophrenia

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October 10, 2019

Part Two: Schizophrenia

Neurotransmitter and Receptor Theories

Neurotransmitter and receptor theories and concepts can be used to explain the occurrences of schizophrenia. Four groups of neurons namely: dopaminergic neurons in the substantia nigra, the cholinergic neurons, noradregernic neurons, and the serotonergic neurons located in the raphe nuclei influence the dynamics of the disease (Heckers, 1997). These neurons often project diffusely to cortical and subcortical regions and regulate the process of transmitting signals. Unlike the expansive search for neurochemical abnormalities in schizophrenia, very few structural studies have shown such systems. For instance, some schizophrenic patients often show brainstem lesions. However, a large fraction of schizophrenic patients often displays glial nodules and perivascular infiltration, which are interpreted as the outcome of a viral infection. In many schizophrenic patients, spatial abnormalities have also been found in terms of patchy fibrillary gliosis, which is maximal with respect to the periventricular and periaqueductal areas. Moreover, significant increase in the cerebral cortex, white matter cortex, and the periventricular structures are associated with schizophrenia. There is a strong relationship between cortical and white matter gliosis with respect to focal brain damage such as degeneration of the substantia nigra, calcification of the hippocampus tumors, and stroke. However, the periventricular gliosis may not be related to the latter (Heckers, 1997). In some schizophrenia patients, the caudate nucleus may show astrocyte density that is like the control cases. Based on the concepts and theories of neurotransmitters, errors that are made by the brain may be rectified. For example, in case neurons in one region of the brain are hypersensitive to the neurotransmitter dopamine, there might be a manner of calming down such hypersensitivity. In the same way, there may be mechanisms of adjusting when there is too much or too little of specific neurotransmitters. This

phenomenon forms the theoretical basis of schizophrenia and other mental conditions such as depression and bipolar disorders. The drugs that are commonly utilized for the treatment of schizophrenia are referred to as antipsychotic medications. However, the identification of specific neurotransmitter receptors that are involved in schizophrenia is often a complex problem. Moreover, each neurotransmitter has various forms of receptors (Heckers, 1997). Furthermore, various types of or combinations of neurotransmitters involved may not be the same for each individual case. Consequently, this problem may result in the need for different antipsychotic drugs each of which addresses various differing forms of neurotransmitter receptors. One of the most challenging concerns to health professionals is the fact that each medication may also affect additional neurotransmitter receptors that may into be involved or associated with schizophrenia.

Symptomology of Schizophrenia

There are various signs and symptoms that characterize schizophrenia. These symptoms take the form of five key domains: hallucinations, delusions, disorganized thinking, grossly disorganized or abnormal motor behavior, as well as negative symptoms. Delusions are common symptoms that take the form of having fixed beliefs that are not amenable to change within the context of conflicting evidences (Shim, Hammonds & Kee, 2007). Delusions may include somatic, persecutory, and grandiose disorder. Persecutory behavior is the feeling that one is going to be harmed, while referential delusions are founded on the belief that certain gestures and talks are directed at oneself. Further, nihilistic delusions are founded on the view that a major catastrophe is in the offing. Hallucinations are symptoms that entail perception-related experiences that take place without an external stimulus (Shim, Hammonds & Kee, 2007). They are usually vivid and clear with a full force and impact of normal perceptions, which are

normally not under voluntary control. Hallucinations may take place on any sensory modality. However, the auditory form of hallucinations is the most commonly observed phenomena among schizophrenic patients. Auditory hallucinations are often witnessed as voices, whether they are familiar or unfamiliar. They are commonly perceived as distinct from the patient's own thoughts and views. The hallucinations may take place within the context of clear sensorium. Further, schizophrenic patients suffer from disorganized thinking or speaking. Also referred to as formal thought disorder, the patients may typically be inferred from the individual speech. The patient may also switch from a single topic to another, a condition referred to as derailment or loose association (Shim, Hammonds & Kee, 2007). Answers to questions may be obliquely related or wholly unrelated. In some scarce situations, speeches may also be severely disoriented to the extent that it is normally almost incomprehensible and resembles receptive aphasia in linguistic disorganization or incoherence. Since mildly disorganized speech may be common and nonspecific, such symptoms may be critical enough to impair effective communication.

Anatomic Changes Observed in the Disorder

There are various anatomical changes that characterize schizophrenic patients. For instance, the entire cortex may reduce significantly in volume. In the same way, the prefrontal cortex undergoes many changes. For instance, the dorsolateral-prefrontal cortex, commonly regarded as the associational isocortical area, such as Brodmann areas, change qualitatively. Such changes may include increased neuronal density. Furthermore, the patient may undergo major enlargements of the fluid-containing ventricles of the brain and the broadening of the fissures that are found between folds of the brain tissues. These changes may take place in degenerative brain conditions. The causes of cerebral atrophy among schizophrenic patients have never been fully established. Considering that the abnormalities are commonly observed in first-

break, acute schizophrenic patients and in chronic situations, it is less likely that the changes stem from the treatment administered. For instance, the atrophies may not be enough indicators of schizophrenia.

Interactions between the Behavioral, Neuroanatomical, and Neurotransmitter Changes

There are various ways in which the behavioral changes in schizophrenic patients are strongly related to neuroanatomical and neurotransmitter changes. For instance, the anomalies that are commonly observed in the frontal cortex, basal ganglia, thalamus, and the cerebellum result in the development of delusions and obsessive-compulsive behaviors. Such interactions often result in major disruptions in the distributed functional circuits as opposed to abnormalities found in single brain regions like the prefrontal cortex. Apart from the frontal cortex, brain anomalies in schizophrenia are also observed in the basal ganglia, thalamus, as well as the cerebellum. There is a strong relationship between behavioral symptoms and the neurotransmitters and neuroanatomical interactions have also been widely observed by researchers. For instance, there is need to explore the cortical and subcortical circuitry in schizophrenia, including the significance of the thalamus and cerebellum in more comprehensive ways (Carlsson, Waters & Carlsson, 1999). For instance, the thalamus may filter out only relevant information and knowledge. As such, the deficits of such functions potentially result in positive symptoms in schizophrenia. This problem may potentially lead to increased lack of clarity of speech due to lack of the ability to filter out important information from the patient's brain. The dopamine hypothesis holds that a dopaminergic hyperfunction in schizophrenia occurs. However, this concept has for a long time been only supported by indirect pharmacological evidences. Usually, chlorpromazine is often synthesized as an effective antihistamine. In the same way, neuroleptics can be linked to dopamine after dozes of reserpine

lead to the same antipsychotic behaviors (Carlsson, Waters & Carlsson, 1999). The reserpine acts by depleting the brain of serotonin and dopamine while chlorpromazine may not affect the levels of such neurotransmitters.

References

Carlsson, A., Waters, N., & Carlsson, M. L. (1999). Neurotransmitter interactions in schizophrenia—therapeutic implications. *Biological psychiatry*, *46*(10), 1388-1395.

Heckers, S. (1997). Neuropathology of schizophrenia: cortex, thalamus, basal ganglia, and neurotransmitter-specific projection systems. *Schizophrenia Bulletin*, *23*(3), 403-421.

Shim, S. S., Hammonds, M. D., & Kee, B. S. (2007). Potentiation of the NMDA receptor in the treatment of schizophrenia: focused on the glycine site. *European archives of psychiatry and clinical neuroscience*, *258*(1), 16-27.

Elaboration of Critical Review

Part Two Assignment: Schizophrenia

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Part Two: Assignment

Overview of Schizophrenia Treatment

The purpose of treating schizophrenic patients is to reduce suffering of the patient and boost their cognitive and social functioning. Lifelong treatment interventions coupled with antipsychotic medications are needed when dealing with many patients. Neuroleptics often work by reducing symptoms of schizophrenia such as thought disorders, delusions and hallucinations, as well as prevention of relapse (Stępnicki, Kondej & Kaczor, 2018). Treatment drugs are also meant to reduce negative symptoms such as social withdrawals and apathy. Patients who suffer from schizophrenia often respond effectively to treatment faster than their counterparts with chronic symptoms. To deter relapses, long-term treatment interventions are often necessary after the first episode of the disease. Dosages that are efficacious in addressing acute schizophrenia need to be ordinarily continued as prophylaxes. Antipsychotic medications are the main drugs that are used for the treatment of schizophrenia.

Classes of Drugs and the Neurotransmitters Involved

There are various drugs that are used to treat schizophrenia. The main drugs are first-generational antipsychotic medications. Antipsychotic drugs act mainly through blocking dopamine D2 receptors that are in the brain. Examples of antipsychotic drugs may include butyrophenones and aliphatic group of phenothiazine derivatives (Advokat, Comaty & Julien, 2018). Aliphatic groups are characterized by explicit sedative effects and moderate extra pyramidal and antimuscarinic side effects. Both typical and atypical antipsychotic medications often react with multiple neurotransmitter receptors. The earlier phase of action of antipsychotic drugs occurs with plasma membrane neurotransmitter receptors. For instance, antipsychotic drugs often bind with a wide range of neurotransmitter receptors such as several forms of

dopamine receptors such as D2, D3, and D4. Usually, dopamine and serotonin pathways are the major regulators of schizophrenia. Apart from these two neurotransmitter pathways, norepinephrine also plays an integral role in mediating the symptoms of depression. The ascending projections also stem from the locus coeruleus of brain stem to the cerebellum, thalamus, hypothalamus, and basal forebrain. Moods, arousals, and cognitions are often regulated and affected by norepinephrine (Advokat, Comaty & Julien, 2018). Descending projections from the spine cord significantly affect pain pathways.

The presynaptic alpha 2 norepinephrine receptors, which are also located on the axon terminals of norepinephrine neurons, operate as gatekeepers for their neurotransmitters. If the norepinephrine's build up in the synapse and binds to the alpha 2 receptors, the additional release of norepinephrine is inhibited. Such receptors play an integral role in modulating the appropriate secretion of norepinephrine (Advokat, Comaty & Julien, 2018). The presynaptic alpha 2 adrenergic receptors, which are normally located on the cell body and dendrites of neurons, are usually regarded as somatodendritic autoreceptors. These elements play a major role in the significant reduction of neuronal electrical activities that result in a shutdown of norepinephrine impulse flow. In the process, there is significant reduction in the amount of norepinephrine that is released at the synapse.

Agonist-Antagonist Actions and Side Effects

Antipsychotic drugs such as loxapine, chloproxazine, and cyamemazine treat schizophrenia symptoms. They act by blocking D2 receptors. However, the excessive blockage of D2 receptors in the hypoactive regions can result in many side effects, such as neurolepsis. Neurolepsis can lead to an extreme kind of slowness or absence of motor movements (Stahl &

Mignon, 2010). This problem may also result in decline in proper functioning of cognitive and affective symptoms. Antagonisms associated with D2 action can occur in the mesolimbic DA pathway. The excessive release of DA within the mesolimbic DA pathway can result in positive symptoms. As such, it is necessary to minimize the actions of DA with the purpose of normalizing the situation (Stahl & Mignon, 2010). The process of administering D2 blocker, which includes conventional antipsychotic drugs, helps to deter DA from binding to the D2 receptor (Advokat, Comaty & Julien, 2018). This form of D2 antagonism potentially results in both the hyperactivity of the pathway and the positive symptoms that are associated with them. D2 antagonism may also take place within the mesocortical DA pathway.

The process of administering D2 blockers within the mesocortical pathway is not often recommended. Due to the hypoactivity of this pathway, which is associated with the negative cognitive symptoms and affective symptoms, symptoms may that be worsened by D2 blockade. Since PFC does not have a high density of D2 receptors, the deterioration of negative symptoms may also stem from a deficient mesolimbic DA pathway. In order to treat both positive and negative symptoms, it is often recommended to reduce DA activities in the mesolimbic pathway and increase DA tone in the mesocortical pathway. Usually, dopamine functions in schizophrenia are not merely too high to low. In some situations, it may be out of tune. Therefore, it should be tuned or regulated sufficiently. Cases of antagonism have also been noted in the nigostriatal DA pathway. The nigostriatal DA pathway is an important component of the extrapyramidal nervous system. It regulates the process of motor control. The nigostriatal pathway seems to be significantly spared in schizophrenia. However, it may induce the motor side effects that are often observed after administering conventional antipsychotic drugs. The absence of DA in this pathway can lead to movement disorders, which may include rigidity, akinesia, bradykinesia, a

well as tremor. Excessive DA in the nigostriatal pathway can result in hyperkinetic movement disorders, which include chorea and dyskinesia. Blockades of D2 receptors, including with conventional antipsychotic drugs, may deter the process of DA binding from there. This situation can result in motor side effects that are usually collectively regarded as extra-pyramidal side effects.

Risk-Benefits for Drug Use

There are various potential risks and benefits that are associated with the utilization of antipsychotic drugs in the treatment of schizophrenia. Considering the potential risks related o the use of antipsychotic medications, in case non-emergent use of such drugs are being considered to address agitation of psychosis, it is important to assess all elements of the evaluation and the treatment plan (Reus et al. 2016). For instance, in case the schizophrenia leads to significant negative impacts to the patient and quality of life, the likelihood for potential benefits of an antipsychotic drug needs to be weighed against their possible harm. This assessment is especially significant considering the modest benefits and demonstrated risks of antipsychotic treatment within clinical trials, and in less rigorous observational and cohort studies. For instance, if there is risk of harm to the patient and others, then acute treatment should be undertaken to allow the immediate crises to be stabilized. Nonetheless, in other situations, the possible benefits and harms with the patient's family members should be discussed.

Long-acting injectable antipsychotic drugs and other long-acting injectable formulations of deaconate are likely to carry a higher risk of side effects in schizophrenic individuals who suffer from dementia. However, schizophrenic individuals with chronic psychotic disorders ma benefit from treatment with long-acting injectable antipsychotic medications in case they have a

history of low adherence or have tolerated oral formulations of the drugs (Reus et al. 2016). In some situations, low dose of long-acting injectable antipsychotic drugs may promote adherence and reduce struggles that are associated with taking of oral medications. Some antipsychotic medications also have metabolites of the parent dug (Reus et al. 2016). Such metabolites may be critical to the process of selecting the medication. For instance, norquetiapine has high anticholinergic side effects than quetiapine.

References

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Reus, V. I., Fochtmann, L. J., Eyler, A. E., Hilty, D. M., Horvitz-Lennon, M., Jibson, M. D., & Wills, C. D. (2016). The American Psychiatric Association practice guideline on the use of antipsychotics to treat agitation or psychosis in patients with dementia. *American Journal of Psychiatry*, *173*(5), 543-546.

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