A Comprehensive Review of the Complexities of Schizophrenia

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PSYC 275: Biological Psychology

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November 28, 2023

Schizophrenia is termed as a “severe, chronic mental disorder characterized by disturbances in thought, perception and behavior”. More loosely, Schizophrenia is thought about as a split or fragmented brain. Schizophrenia has been deeply researched as a central point of clinical investigation and is one of the most intriguing and challenging subjects of psychologists. As a multifaceted condition, it defies easy categorization and comprehension due to the countless amount of symptoms that vary widely across individuals. Even though Schizophrenia is a rare condition, with only 24 million people diagnosed across the world, the comprehensive understanding of Schizophrenia serves as a requisite for clinical research but also is useful for combating prevailing stigmas that have been prevalent in society. This is seen through the barbaric and inhumane treatment options that have been utilized since the 1940’s. Those who exhibited symptoms of Schizophrenia were not only majorly misunderstood, but institutionalized and sometimes even persecuted.

Schizophrenia has various characteristics, including both positive and negative symptoms. Positive symptoms of Schizophrenia reflect an excess or distortion of normal function, including auditory and visual hallucinations and delusions. Negative symptoms reflect the absence of normal behaviors related to motivation and interest, including affective flattening, anhedonia, asociality, alogia, and avolition. When diagnosing Schizophrenia, negative symptoms are a core component of Schizophrenia that account for a large part of the long-term disability and poor functional outcomes in patients with the disorder; however, “since some patients may lack insight about the presence of negative symptoms, these are generally not the reason that patients seek clinical care, and clinicians should be especially vigilant for their presence” (Correll & Schooler, 2020). There are also severe cognitive impairments that occur in the earliest stages of Schizophrenia. Through neurocognitive studies, it was displayed that people experiencing their first episode of Schizophrenia had significantly worse performance on all cognitive measures than healthy controls and struggled the most with processing speed and with verbal learning and memory, especially when encoding information; their measured IQ and

other cognitive abilities also dropped the most between the high-risk period just before symptoms appear and the first acute phases (Mesholam-Gately & Giuliano, 2009). This exhibits the severity of Schizophrenia's cognitive impairment and how it affects memory, executive functioning, and attention, thus showing how it often leads to significant impairments in social and occupational functioning. Individuals may struggle to maintain relationships and employment which leads patients to turn to medication and other forms of treatment.

Schizophrenia is not as common as other mental disorders and affects approximately 24 million people or 1 in 300 people (0.32%) worldwide, according to the World Health Organization. Even with its low prevalence across the world, Schizophrenia has many serious effects. It's seen that patients with Schizophrenia are more likely to experience premature mortality. This is due to many causes including co-occuring medical conditions that are not treated, as well as suicide. An estimated 4.9% of people with Schizophrenia die by suicide, which is a staggering percentage compared to the general population suicide rate, contributing to the highest risk in the beginning stages of an illness (Palmer et al., 2005). There is also an acute gender difference in those being diagnosed with Schizophrenia, with it being more prevalent in males than females. The onset of symptoms also differ with gender; in females, onset is typically later (often in their twenties to thirties) compared to males (often in their late teens to early twenties). Hormonal factors may also contribute to gender differences due to the role of estrogen having a protective effect, thus potentially influencing severity in symptoms, particularly during the menstrual cycle.

The direct and exact causes of Schizophrenia are still unknown. There are three theories of the etiology of Schizophrenia, including genetic, neurodevelopmental, and neurobiological, though these theories are not completely separate from each other (Kim, 2016). The heritability of Schizophrenia is reported to be around 80%-85%. The neurodevelopmental theory is centered around the genetic linkage, pathogenic occurrences, and various environmental factors including adverse environments during the perinatal stage. The most promising theory is

the neurobiological theory which addresses the abnormalities of structures and functions in the brain. There are many neurobiological abnormalities that are seen in patients with Schizophrenia, such as impaired functional connectivity in the prefrontal cortex, neurotransmitter abnormalities, and reductions in white and gray matter structures to name a few. The neurobiology theory is helpful in understanding the course of Schizophrenia and how it may progress.

There are many neurobiological causes of Schizophrenia, beginning with severe brain impairments. In patients with Schizophrenia, there are enlarged ventricles and reduced cortical thickness, loss and disorganization of cells in the hippocampus, as well as decreased volume of gray matter in the putamen and thalamus. In addition to this, it's also important to look at the level of dopamine release which can help guide patients towards the best treatment option or medication. A high level of dopamine in the nucleus accumbens and striatum drives hallucinations, whereas a low level of dopamine in the prefrontal cortex drives negative and cognitive symptoms. Hypofrontality, or reduced activity of the prefrontal cortex, leads to poor planning, problem solving, and attentional set shifting, all of which are cognitive impairments in those with Schizophrenia. Deficiencies in glutamatergic neurotransmission are due to NMDA receptor deficiencies. We see this through how NMDA antagonists, such as PCP and ketamine, induce positive and negative symptoms. There is evidence of altered connectivity between different brain regions in schizophrenia. Neuropsychologists have also related smaller sizes in two distinct webs of brain fibers to two distinct types of cognitive malfunction; brain images from the schizophrenic patients showed abnormalities in two functionally and anatomically different neural pathways - the uncinate fasciculus and the cingulate bundle (Nestor et al., 2004).

Schizophrenia is an illness that has been treated in many extreme ways over time, demonstrating the severity of Schizophrenia's symptoms. In ancient times, trepanation was used and in medieval times, lunatic asylums were utilized. In the 1940's, insulin shock therapy was used on patients in an infirmary ward which resulted in sedation, sweating, violent and

frantic crying, dilated pupils, with a coma following the “symptoms of excitement” (Larkin & Sydney, 1937). First generation antipsychotics were D2 antagonists which led to a reduction in positive symptoms. However, these antipsychotic medications produced extrapyramidal symptoms including weight gain, sedation, dry mouth, dystonia, Parkinsonism, tardive dyskinesia, and hyperprolactinemia. Since the 1990’s, atypical antipsychotics have removed the dopamine level slightly and target serotonin receptors while also removing affinity. This allowed negative symptoms to also be targeted while reducing the extrapyramidal symptoms from the first generation antipsychotics; even so, 20%-30% of people do not respond. While antipsychotics focus on taming the positive and negative symptoms, cognitive impairment is also common in Schizophrenia as discussed earlier. It was shown that there are still mental deficits in Schizophrenia patients even if psychological symptoms are addressed. Cognitive remediation was used in a study to target cognitive deficits; the results show that providing cognitive remediation in addition to psychiatric rehabilitation contributed to greater improvement in both cognitive and social functioning than psychiatric rehabilitation alone (Iwata et al, 2017). This shows how cognitive remediation may enhance the efficacy of psychiatric rehabilitation which improves social functioning. This displays the growth of medication but also how treatments aside from medication can help target symptoms.

Future research should look at prevention, due to Schizophrenia occurring later in adolescence. This could be looked at through neurobiological mechanisms and how genetics as well as specific neurotransmitter systems could be potentially altered with medication which could influence brain development. Imaging techniques and biomarkers that could be used in early detection would greatly improve chances of mitigating the progression of Schizophrenia. In addition to this, because environmental factors can increase the risk of Schizophrenia on top of neurobiology and genetics, examining the role of specific triggers and social determinants in individual cases will also help on the prevention and early detection front.

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