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Holistic Solutions to Schizophrenia Management in Geriatric Populations

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ABSTRACT

Schizophrenia is a psychiatric condition characterized by dysfunction in thoughts, behavior, and emotions. The illness is typically diagnosed in late adolescence to early adulthood, and generally lasts throughout a patient's lifetime. This debilitating condition affects approximately 25% of adults aged 55 years old and older. With numbers of elderly adults afflicted by psychiatric illnesses increasing in the future, special precautions need to be taken to address this underserved population. This increase in schizophrenia frequency among elderly populations also has repercussions not just for future healthcare, but health costs as well, with schizophrenia expenses being costly in comparison to other psychiatric ailments. A major theory explaining the genetic and physiological basis of schizophrenia is the dopamine hypothesis, which describes a disruption in the normal transmission of the dopaminergic pathway as well as the mesolimbic system. Current treatments of schizophrenia often involve pharmacological interventions that create heightened side effects in the elderly. There is a need for more research into efficient and effective treatments for the future, especially treatments that can be safe for elderly use such as brain stimulating interventions. Destigmatizing mental health issues and advocating for safer and more efficient therapies are the key to improving outcomes of geriatric schizophrenic patients.

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Introduction

Schizophrenia currently impacts approximately 1% of adults globally and 0.6% to 1.9% of adults in the United States [1]. By 2050, the prevalence of schizophrenia in older adults is predicted to reach 1.1 million people in the U.S. and 10 million people worldwide [2]. Among people aged 60 years or older, schizophrenia ranks third as the reason behind causes of disability adjusted life years [2]. Disability adjusted life years (DALY) are the number of healthy years someone will lose in their lifetime, due to a combination of years lost by premature mortality, or years of life lost (YLL) and years lost to disability (YLD) [3]. Schizophrenia is typically diagnosed in early adulthood. However, as more individuals with schizophrenia age, individuals 55+ years old will encompass 25% or more of the total cases [2].

The number and proportion of these elderly schizophrenia patients are potentially slated to increase in developed countries. The future demographics of modernizing countries are shifting towards a larger subset of older adults due to increasing life expectancy and decreasing fertility rates [4]. By 2050, the global elderly population (age 60 and older) is expected to reach two billion and exceed the number of children and adolescents under the age of 14 [5, 6]. This positive trend of life expectancy in low-mortality countries has been ascribed to the declining mortality rates of older adults [7]. Further, the percentage of older people with major psychiatric disorders is also expected to increase as the population in the USA and similarly developed countries ages [8]. By 2030, the number of people over 65 with a major psychiatric disorder will be roughly equal to those aged 30 to 44 with a similar disorder [8]. As the prevalence of oft-conflicting

literature on psychiatric disorders increases each year, so rises the importance of performing truly comprehensive systematic reviews on each psychiatric disorder of interest to synthesize and build on latest findings. The use of machine-learning text-mining software such as SWIFT-Review may prove useful in this regard [9, 10].

These expected trends create widespread implications for future health costs, especially given that older adults with schizophrenia have greater expenditures per person than those with most other medical or psychiatric disorders. One study found that expenditures for older adults with schizophrenia were $11,304 higher per person than for depression and $28,256 higher per person than for other medical conditions [11, 8]. These implications are particularly concerning because only 1% of current literature about schizophrenia addresses this age-specific population, demonstrating the lack of adequate public attention to this issue [2]. Thus, this paper will discuss the etiology of schizophrenia, symptoms, onset, treatment, and the unique challenges or costs that addressing this condition in the elderly pose.

Schizophrenia Etiology

Schizophrenia is a complex behavioral and cognitive syndrome characterized by periods of disturbed behavior and psychosis that can cause considerable social impairment [12]. The etiology of schizophrenia is still unknown, but the condition is believed to be related to a combination of genetic and environmental disruption to the brain [13, 14]. Evidence supporting this is consistent across multiple monozygotic (identical) and dizygotic (fraternal) twin studies conducted in the last century. These studies reveal a 40% to 50% concordance rate in monozygotic twins, which is greater than that in dizygotic twins, and an 80% estimated rate of heritability. Further, studies including the offspring of both affected and unaffected monozygotic twins display a similar risk of schizophrenia and schizophrenia-related disorders, and suggest that unaffected twins, in fact, carry a genetic risk for schizophrenia, despite expression of the disease. These results support theories pertaining to epigenetics and non-shared environments [15, 16, 17].

Genes associated with schizophrenia include neuregulin 1 (NRG1), dysbindin-1 (DTNBP1), and catecholamine O-methyltransferase (COMT) [18, 19, 20]. NRG1 is involved in glutamate signaling and brain development, DTNBP1 functions in glutamate release, and catecholamine O-methyltransferase (COMT) is involved in dopamine regulation [18, 19, 20].

The dopamine hypothesis is a major theory that attempts to explain the pathophysiologic mechanism underlying schizophrenia. It suggests that abnormal transmission in the mesolimbic dopaminergic pathway is associated with the positive symptoms of schizophrenia, while abnormal transmission in the mesocortical dopaminergic pathway is associated with the negative symptoms [21]. The mesolimbic pathway consists of dopaminergic neurons that project from the ventral tegmental area into the ventral striatum [22]. Also labeled as the "reward pathway," the mesolimbic pathway plays a central role in reward and motivation, but is also involved in pain modulation, sensation, and perception [20]. Abnormalities in this pathway have been linked to other mood-related disorders including, but not limited to, bipolar disorder and major depressive disorder [23]. The mesolimbic pathway is of particular interest in schizophrenia, as the ventral striatum has been shown to play a critical role in the disease and therefore serves as a potential drug target [21]. Task fMRI studies have shown a correlation between activity alterations in the ventral striatum, which is essential in reward based learning and emotional processing, with negative symptoms of schizophrenia [24]. Moreover, loss of cholinergic interneurons in the striatum have been hypothesized to cause mesocortical dysfunction [25].

Despite this evidence, newer studies suggest that factors outside of the dopamine hypothesis may also play a role in the onset of this disease [1]. First, serotonergic, alpha-adrenergic, and dopaminergic hyperactivity or GABA and glutaminergic hypoactivity have been implicated in schizophrenia symptoms [1]. Secondly, abnormal neuronal connectivity - possibly involving interneurons - may impact etiology, but its exact mechanism, timing, and location are uncertain [12].Thirdly, a number of socioeconomic, environmental, and genetic factors are associated with the disease, including preeclampsia, emergency cesarean section, birthing complications, unusual fetal development, gestational diabetes, low birth weight, maternal malnutrition, vitamin D deficiency, winter birth (associated with a 10% higher risk of schizophrenia), and urban residence (associated with a 2% to 4% higher risk of schizophrenia) [1]. Recent longitudinal studies have also suggested a 40% increased risk between cannabis use and psychosis, suggesting a dose-dependent relationship [1].

The risk of schizophrenia may also vary depending on ethnic and social status [1]. For instance, an epidemiological study in Britain demonstrated a higher incidence rate by up to tenfold in the children of African and Carribean migrants in comparison to those in the general population [1]. Another study demonstrated how predominantly black immigrant groups in Western Europe experienced markedly increased rates of schizophrenia [26]. In fact, African Americans were three times more likely than Caucasians to be diagnosed with schizophrenia. Nevertheless, the prevalence of schizophrenia appears to be similar in men and women [27].

Schizophrenia Symptoms

Primary symptoms of schizophrenia are typically divided into three categories: positive, negative, and cognitive symptoms [28]. Positive symptoms include psychotic manifestations such as hallucinations and delusions [29]. Negative symptoms include avolition, emotional blunting, loss of thought and behavior, blunted affect, and lack of speech and communication [30]. Lastly, cognitive symptoms include impairment of memory, attention, and executive function [31].

Positive symptoms will oftentimes relapse and remit while negative symptoms tend to persist chronically [12]. The first episode of psychosis typically manifests during late adolescence or early adulthood and is predated by an unusual mental risk state or prodromal period [12, 32, 33]. Sometimes, individuals with the disease demonstrate impairments in mental and social functioning several years prior to onset of the disease [34]. Even so, schizophrenia can present without prodrome in previously well-functioning adults [12]. In cases of cannabis use, 11% of individuals experienced generally open, positive, and sudden symptoms within the first year [35].

Onset of Schizophrenia

While the onset of schizophrenia typically occurs during the third decade of life, this condition can also present with early-onset (13 to 18 years old) and late-onset (after the age of 44 years old) [36]. Late-onset schizophrenia accounts for 15% to 20% of all cases of schizophrenia, typically when patients are middle aged. Very late-onset schizophrenia, which occurs after age 65, typically follows conditions of dementia and other neurocognitive disorders [8]. These individuals tend to have better premorbid functioning

and fewer negative symptoms and neurocognitive issues. Women tend to present with late-onset schizophrenia more commonly than men [20]. Furthermore, recent studies have shown that older patients experience an improvement in their symptoms as they age [37]. In comparison to younger patients, they have fewer positive symptoms, although their negative symptoms tend to remain throughout life [38]. Late-onset schizophrenia patients require lower doses of antipsychotics compared to those with earlier onset [9].

Schizophrenia in the Elderly

The schizophrenic population is divided into two subgroups of older individuals: "young old" (ages 55 to 74) and "old-old" (age 75 and up) [2]. These two groups include individuals with late-onset schizophrenia, as well as individuals with early-onset schizophrenia whose condition progresses until late in life. The risk of mortality is two to three times greater in patients with schizophrenia than in the general population and this trend has been increasing over the past few decades [2]. Older adults with schizophrenia face above average rates of mortality due to suicide or accident. Moreover, older people with schizophrenia face higher rates of health conditions such as chronic obstructive pulmonary disease (COPD), hypothyroidism, and congestive heart failure. Individuals with schizophrenia are also more likely to engage in unhealthy behaviors such as poor diet, lack of exercise, smoking, and refusal of medication [39]. Additionally, taking second generation antipsychotics increases the likelihood of experiencing weight gain and metabolic syndrome. As a result, these individuals are subject to a 2- to 3-fold increase in cardiac mortality and 2-fold increase in all-cause mortality, potentially exacerbating disease burden [40].

Addressing Mental Health in the Elderly

Mental health conditions may limit the ability of elderly individuals to live autonomously, perform basic everyday activities, and maintain quality of life [6]. However, mental health problems are often left undiagnosed and untreated in the elderly. Depression and memory loss are oftentimes overlooked or misclassified by clinicians as normal signs of aging. Due to stigma, many elderly people also tend to deny experiencing problems and regard mental illness as a sign of weakness [41]. Although the number of older adults suffering from mental illness is estimated to be between 10.1 and 14.4 million individuals by 2030, it is likely that the true number is much higher due to the large number of undiagnosed cases each year [42].

Furthermore, there is a lack of resources available to elderly populations with mental health issues and an insufficient number of mental health providers with specialized training in care for older adults [41, 11]. As a consequence of this lack of training, health professionals may inadvertently exhibit ageism in the form of stereotyping, prejudice, or discriminatory behaviors against older adults [43]. Studies have shown that physicians are less likely to involve their older patients in medical decision-making than their younger patients. Clinicians have also shown to be less patient, involved, respectful, and optimistic when addressing older patients [44]. Health professionals tend to view older peoples' conditions as stagnant and unlikely to improve, and consequently may limit the treatment options that they present to their patients [6]. Their biases and pessimism lead them to believe that efforts to administer psychiatric care to the elderly would be futile: older people cannot change and it is too late to provide care [6]. As a result of these tendencies and perspectives, little investment has been made in policies that create programs for the elderly suffering from mental health issues [6].

Decision Making Capacity in Elderly Patients with Schizophrenia

Appropriate treatment of elderly patients with schizophrenia comes with unique challenges [8]. Patients are asked for routine consent for antipsychotic medications; however, schizophrenia may deprive patients of their cognitive ability to independently form decisions [45]. This issue is further complicated in older patients with schizophrenia who may suffer with a comorbidity such as physical frailty, which makes patients less likely to tolerate harsh side effects from medications; informed consent is thereby especially important in the treatment process [8]. Indicators of impaired decisional capacity include cognitive deficits and, to a lesser degree, the severity of negative symptoms [46].

In order to ensure that their patients have sufficient cognitive capacity for consent, health professionals recommend utilizing the MacArthur Competence Assessment Tool for Treatment (MacCAT-T) [47, 48]. This 15 to 20 minute interview assesses the patient's ability to understand the nature of his or her treatment, as well as its risks, benefits, and alternative solutions [49]. The patient should also be able to demonstrate a clear and consistent choice when choosing his or her options.

In cases where patients cannot regularly demonstrate consent, patients may have their power of attorney transferred to another person, usually a spouse or family member [50]. Since not all patients have power of attorney documentation, it is important that patients and physicians have critical conversations about end-of-life care and management when patients are able to have these discussions [51].

Treatment

The current treatment of schizophrenia involves a combination of antipsychotic drugs, psychological therapies, and brain stimulation devices [12, 52]. However, there is a growing need for safer and more efficient treatments as current options are proven to be limited in efficacy and may not prevent life-threatening effects of the disease. There has recently been progress in genomics, neuroscience, and epidemiology; however treating the disorder still poses many challenges [53].

Pharmacotherapy

Older adults may experience greater adverse effects in response to antipsychotic medication due to physiological changes that occur with aging [54]. The blood brain barrier serves as an important interface between the brain and other body tissues, but as individuals age, inflammation and loss of tight junctions without leukocyte recruitment leads to disruption of the blood brain barrier [55]. When the blood brain barrier increases in permeability, a higher dosage of medication is able to enter the brain. Since elderly adults experience stronger side effects to medication, health professionals should consider administering antipsychotics at dosages lower than those given to younger persons [56].

Current treatment of schizophrenia consists of first (dopamine D2 receptor antagonists), second (multi target antagonists, with a larger emphasis at the serotonin 5HT2A receptor than dopamine D2 receptor), and third generation antipsychotics [57]. Third generation antipsychotics include drugs such as aripiprazole, brexpiprazole and cariprazine, each of which possesses unique mechanisms [58]. For example, aripiprazole can act as both a partial agonist or antagonist to dopamine D2 receptors [59]. Aripiprazole additionally serves as an antagonist or partial agonist for the β-arrestin-2 signaling pathway; β-arrestins are broadly involved in regulation of desensitization and internalization of many GPCRs [60, 61].

Social Skills Therapy

Elderly patients with schizophrenia may experience dangerous side effects to antipsychotics due to their heightened response to drugs [62]. Therefore, patients should explore non-pharmaceutical interventions. Evidence has shown that supportive psychotherapy may have a positive, but modest effect on the cognitive deficits seen in schizophrenic patients [63]. Psychotherapy includes social skills training, which utilizes behavioural techniques to teach individuals how to communicate their emotions and requests appropriately [64]. Sessions involve model learning or role playing in order to enhance people's abilities to perform eye contact, gestures, and fluid speech. Additionally, these programs teach patients how to manage negative emotions and provide positive feedback to others [65]. People with schizophrenia are more likely able to adjust to varying social settings and live independently with the help of psychotherapy [66].

Brain Stimulation Therapy

Neuromodulatory treatments, such as electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS), pose safer and more effective alternatives to elderly patients with medication-resistant schizophrenia [67]. ECT induces seizures in the human brain using small electrical currents [68]. Although ECT is not effective in treating negative symptoms, it significantly improves positive symptoms, such as catatonia, and overall morbidity [67]. On the other hand, TMS has shown to be successful in targeting medication-resistant negative symptoms and auditory hallucinations. TMS modulates the brain's electrical activity by utilizing strong, alternating magnetic fields which traverse throughout the scalp and skull [69]. This treatment is safe and well received by patients [69]. Additionally, combining TMS and ECT may create a powerful synergistic therapy in the future [67].

Expenses

Schizophrenia is one of the most expensive disorders to treat with costs increasing across rising age cohorts [11, 70]. In a previous study, researchers found that among people aged 65 and older, treating patients with schizophrenia cost $40,000 annually per person. This cost is higher than the treatment of elderly patients with depression, dementia, or physical illness [8]. The cost of this schizophrenia treatment is approximately 50% greater than the cost of treatment for patients with depression and approximately three times higher than that for patients with physical illnesses [8].

For younger patients (ages 19 to 44) with schizophrenia, half of the annual expenditures ($10,244) were spent on outpatient mental health services [8]. However, once the patients turned 75 years old and older, outpatient services consumed only 5% of annual expenditures. Treating patients for schizophrenia in old age became markedly more expensive due expenditures for nursing home care, which amounted to $28,395 or 83% of total costs. The significantly larger medical costs for elderly individuals with schizophrenia demonstrate the level of disability they experience from a combination of cognitive dysfunction and declining health [8]. In order to decrease costs related to nursing homes, future projects should address ways to improve cognitive functioning and autonomy in these patients.

Discussion

The current demographic trend points to a massive future challenge involving public health policies for the elderly. Significant contributions to this future challenge are major health issues which tend to accompany aging, including chronic disease (e.g. hypertension and arthritis), functional disability and cognitive impairment [71]. Cognitive dysfunction, such as in elderly patients with schizophrenia, is of particular concern because impaired mental health may limit patients' ability to live independent lives and cause them to accrue significant healthcare related costs.

Taking care of this growing, aging population will be expensive and logistically difficult [5]. The younger population in comparison will be growing at a slower rate, placing additional pressure on the current labor force, nursing homes, government resources, and healthcare services. However, efforts to destigmatize mental health may encourage older patients to be more willing to seek treatment for their condition. Furthermore, if safer therapies are provided that reduce symptoms with fewer side effects, patient quality of life may be improved even further. Lastly, if social and cognitive awareness programs can be expanded properly, many more patients may regain the skills to live independently. The effects of these clinical and social efforts will be felt beyond schizophrenia, improving outcomes from other forms of mental illness prevalent in geriatric populations.

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