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Older Adults with First-Onset Schizophrenia: An Under-Recognized and Under-Served Patient Population

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Abstract

Schizophrenia is typically understood to be a disorder with onset in early adulthood, but nearly a quarter of patients are estimated to develop schizophrenia after age 40. Late-onset schizophrenia (patients with onset after age 40) and very-late onset schizophrenia (patients with onset after age 60) are historically an under-recognized and under-served population. Reasons for this are manifold and may include barriers such as inconsistent terminology used to describe these patients, challenges with diagnosing, and a lack of research and resources for these patients. To overcome these barriers, field studies should be conducted to determine if diagnostic manuals should include these subsets and thus provide clear diagnostic criteria. With clear criteria learning objectives could be made for medical school and residency programs which would promote the recognition of these patients. Clear diagnostic criteria would also help clinicians differentiate between onset of schizophrenia in later life and psychosis as a result of another cause such as dementia or depression. Finally, allocating funds towards research and resources in first-onset diagnosis of schizophrenia in adults over 40 would lead to the creation of evidence-based treatment guidelines for this population and allow advocacy for this poorly defined but vulnerable patient population.

Keywords: Schizophrenia• Psychosis• Geriatric psychiatry• Health services for the aged

Abbreviations: ICD: International Classification of Disease; DSM: Diagnostic and Statistical Manual; EOS: Early-Onset Schizophrenia; LOS: Late-Onset Schizophrenia; VLOS: Very-Late Onset Schizophrenia; (V) LOS: Both Late-Onset Schizophrenia and Very-Late Onset Schizophrenia

Introduction

Schizophrenia is a chronic and debilitating mental health disorder characterized by prominent psychosis and functional decline. While it is classically understood to be a disorder with onset in early adulthood, nearly a quarter of patients are estimated to develop schizophrenia after age 40 [1]. Although similar to younger-onset cases, older-onset schizophrenia is associated with a predominance in women, better premorbid occupational and social functioning, hallucinations of all sensory modalities (i.e., visual, tactile and olfactory as opposed to just auditory), and deprivation syndromes such as hearing and visual loss (especially among patients over age 60) [2-5]. In addition, delusions are commonly persecutory in nature in older patients and there is a higher rate of paranoid symptoms [6]. Information on other risk factors and clinical presentation characteristics may be limited, as these patients are said to be poorly understood and under-recognized [7].

Since the number of older adults with first-onset schizophrenia is expected to increase as the population ages, healthcare workers will need to prepare accordingly by enhancing their awareness of this entity so that effective treatments can be implemented [8, 9]. Over the years, barriers such as inconsistent terminology, diagnostic ambiguity, and limited research, treatment, and resources have resulted in making this subset of schizophrenia historically under-served. This paper will address these barriers in detail and propose possible approaches for improvement that would aid healthcare workers in better caring for these patients.

Historical Overview of Schizophrenia Terminology

Schizophrenia onset in older adults is not a newly discovered phenomenon; in fact, it was clinically recognized as early as the mid-20th century [7,10]. Unfortunately, wording and labels used to describe schizophrenia have shifted throughout the years, especially with regards to different age groups, thereby creating a climate of ambiguity as well as a lack of recognition of its prevalence in older adults [11,12]. To expand on this further, the following section will provide a brief historical overview of schizophrenia terminology and how it has evolved.

When schizophrenia was first described in 1893 by the German psychiatrist Emil Kraepelin, he used the term "dementia praecox," to denote an illness that affected predominantly young adults, thus giving rise to a misconception that persists to this day [13]. However, later in his career, Kraepelin conceded that onset was not limited to youth, and that his initial choice of nomenclature was inaccurate [14]. Furthermore, the Swiss psychiatrist, Manfred Bleuler, who is arguably considered the "founding father" of schizophrenia onset in older adults, coined the term "late-onset schizophrenia" in 1943. This came about after thoroughly studying over 100 patients whose onset occurred at age 40 or older. His patients presented similarly to those of Kraepelin, but were less likely to exhibit negative symptoms such as affective blunting and formal thought disorders, and tended to have a more benign course of illness [1,10].

In 1952, English psychiatrists Roth and Morrissey replaced the term "late-onset schizophrenia" with "paraphrenia," which was later incorporated into the ICD-9 [5,15]. According to medical historians, this change gave rise to great confusion, as the term "paraphrenia" was originally used by Kraepelin to designate an illness distinct from schizophrenia [5,11,14]. Consequently, the change in the ICD-9 perpetuated the false idea

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that schizophrenia does not develop in older adults. In 1980, the DSM-III furthered this misconception by including "onset prior to age 45" as a diagnostic criterion for schizophrenia [16]. Although this criterion was removed in 1987 with the revised version of the DSM-III (DSM-III-R), the confusion and debate persisted [7,12,17].

Clarity arose at the turn of the century, when Howard et al. of the International Late-Onset Schizophrenia Group (ILOSG) published a consensus report outlining three major classifications of schizophrenia based on age group: early-Onset Schizophrenia (EOS) was defined as onset prior to 40 years of age; Late-Onset Schizophrenia (LOS) with onset after age 40, and Very-Late Onset Schizophrenia (VLOS) with onset after age 60 [5]. By establishing clear nomenclature and age cut-offs, the ILOSG consensus represented a pivotal step in the recognition of schizophrenia onset in older patients. However, the categories of EOS, LOS, and VLOS have yet to be incorporated into the DSM or ICD, which would be a necessary step in order to optimize the diagnosis of first-onset schizophrenia in older age. DSM diagnosis is validated by field studies which look at diagnostic clusters to determine longitudinal stability-the consistency of diagnosis between interviewers over time. Therefore, inclusion of these categories into field studies would be the first step towards implementing these subtypes into the DSM. Conducting these field studies and subsequently including these older-age subtypes into the DSM would likely help to spread awareness of the older-age subtypes among the large audience of DSM readers, and thus a longstanding pattern of inconsistent terminology may finally reach resolution [18].

Diagnostic Ambiguity

Despite the consensus reached in 2000 regarding the three subtypes of schizophrenia, the validity of these classifications remains in dispute, likely perpetuating the lack of recognition and misdiagnosis of older patients [11]. Further, due to overlap in clinical presentations, it can be confusing for clinicians to differentiate between schizophrenia and other types of psychoses, such as those that occur as a result of dementia. The following section will further discuss the debate regarding the diagnostic validity of LOS and VLOS (collectively referred to as "(V)LOS") and will discuss their differential diagnoses.

Many researchers remain skeptical with regards to the legitimacy of (V)LOS diagnoses [18-21]. It is important to note that having a diagnosis based on age without a persuasive rationale for the specific cut-off is rare in medical nosology, and that the three groups should ideally have characteristics that are age-associated with a distinct natural history and comorbidities associated with each [18]. Stability of diagnosis would be important for validation, and thus longitudinal data would be important to obtain.

Additionally, many researchers argue that onset of schizophrenia in older age many simply be a prodrome of dementia, as the literature shows higher rates of dementia among these patients compared to individuals with EOS and healthy controls [7,18-21]. A one five-year follow-up study of patients with LOS found that nearly half of the patients had developed dementia [22]. It remains highly debated as to whether older adults who develop schizophrenia are validly diagnosed or whether they are simply a higher risk for developing dementia in the first place, but there is ample evidence to suggest the latter. In Howard et al.'s study in 2000, more than half of the participants may have had a mild cognitive impairment (based on MMSE scores), which is a major risk factor in the development of dementia [5,18]. In addition, research on cognitive functioning in (V) LOS patients and studies on brain imaging and biomarkers suggest that schizophrenia onset at a later age is distinct from dementia and does not incur a causative effect [5,23-26].

Compared to patients with dementia, both LOS and VLOS patients exhibit overall superior cognitive functioning and less cognitive decline. Areas of cognitive deficits, when present, are different from those of

dementia patients. The literature suggests that VLOS patients have poorer attention skills compared to patients with Alzheimer's Disease (AD), but have superior memory and learning functions [27]. In addition, the cognitive changes that take place in both LOS and VLOS groups have been shown to resemble those of EOS patients, reinforcing the notion that these are subsets of the same illness [27-29].

On a similar note, brain imaging studies of patients with (V)LOS reveal comparable microstructural changes to those seen in patients with EOS [5]. In contrast to AD brain imaging, these studies did not find significant limbic tauopathy or amyloid deposition in patients with either LOS or VLOS, and pyramidal cell numbers in the hippocampus were preserved [30,31]. Supporting this, a study measuring concentrations of biomarkers (tau and beta-amyloid) in the Cerebrospinal Fluid (CSF) of elderly patients with late-onset psychosis found that none of the patients with VLOS had a CSF profile typical of AD [25].

In addition to recognizing the validity of LOS and VLOS diagnoses, it is important to be able to differentiate these subsets of schizophrenia from psychoses due to other illnesses. Hallucinations and delusions can arise in the elderly for a number of reasons. The differential is vast, and includes major depressive disorder, bipolar disorder, sensory deficits, polypharmacy, substance intoxication and withdrawal, medical disorders, dementia, etc. [32]. One particular clinical challenge commonly discussed in the literature is recognizing the difference between (V) LOS and dementia. Neurocognitive testing using the Montreal Cognitive Assessment (MoCA) or the Mini-Mental State Examination (MMSE) may be helpful, as patients with both LOS and VLOS tend to score higher than patients with dementia. However, this is not useful for patients who have concomitant dementia and (V) LOS, or for patients in whom Lewy Body Dementia is suspected [26,28]. An accurate diagnosis, guided by a full physical exam, history (with collateral), and review of medications is critical for every patient with psychosis in order to make the necessary differentiation and subsequently provide effective treatment [12]. Brain imaging should also be obtained if available [5]. To facilitate the diagnostic process, clearer diagnostic guidelines should be established in order to help clinicians differentiate between (V) LOS and dementia and to help subtract the effects of physical comorbidities. In addition, to further support recognition and awareness of these patients, incorporating the subject of older-onset schizophrenia (including the subsets EOS, LOS, and VLOS) into the learning objectives for medical schools and residency programs may ultimately lead to better recognition, advocacy and treatment for these patients.

Limited Research, Treatment, and Services

Due to the age cut-offs in the DSM-III, North American research prior to 1987 excluded patients who developed schizophrenia later in life, which has resulted in fewer overall studies on the subject to this day [33]. Some progress has been made, as the nomenclature established by Howard et al. generated interest in the research community. However, a search on Pubmed and CINAHL using terms such as "late-onset schizophrenia", "very-late onset schizophrenia", and related terms reveals few results compared to those of "early-onset schizophrenia" [7]. In terms of treatment, low-dose amisulpride, an antipsychotic known for its lack of sedating effects, has been shown to be well-tolerated for patients VLOS, but there are overall very few evidence-based randomized clinical trials on which to base treatment guidelines for older patients who develop schizophrenia [34,35]. Without sufficient studies on this patient population, treatment of these subtypes will remain limited. However, it is useful to extrapolate from general knowledge of treating the geriatric psychiatry population; the mantra of "start low and go slow" is important to follow in the context of pharmaceutical treatment when it comes to older-onset schizophrenia. Non-pharmacological interventions such as CBT and supportive therapies should also be implemented whenever possible [18,36].

Lack of available services is another key barrier to properly caring

for (V) LOS patients. Early intervention programs have been invaluable in the treatment of schizophrenia in youth patients, improving recovery rates and simultaneously reducing relapses, suicides, and overall costs [37,38]. However, most programs in the Canada, US, and UK have age cut-offs at 35, thus excluding both older-age subtypes from participation. Reasons for this inequity are multifold. Firstly, needs of the older-onset groups differ considerably from the younger-onset groups, as most of them have already achieved adult-roles (career, family, etc). Secondly, some speculate that youth may derive more benefit from programs that are geared specifically towards them and their needs, and extending the age range would dilute this focus (although, one could argue that many of the services provided by these programs are not age specific). Lastly, older patients are more likely to have medical comorbidities and may require more extensive nursing care and management than these current programs are equipped capable of providing. In the interest of better serving this patient population, creating early intervention programs specifically geared towards treatment of (V) LOS patients would be a possible solution worth exploring [39].

Extending research and services to include more patients with (V) LOS is an obvious solution to overcoming the barrier of insufficiency observed in these areas. Unfortunately, the lack of these resources is only one aspect of the problem. In studies where early-onset programs were made available to older patients, only a small proportion actually accessed them [39]. In addition, when these patients do participate in research studies, they are often lost to follow-up [40]. Reasons for the lack of participation are unclear, but social isolation may play a role, as this is known to be common among (V)LOS patients prior to diagnosis, and the experience of delusions in schizophrenia may lead individuals to withdraw even further [21,41]. With respect to VLOS patients specifically, it is notable that the stigma of mental illness remains prevalent among all functional mental illness in the elderly (i.e., mood disorders, anxiety disorders, psychotic disorders, etc.), in contrast to organic mental illnesses such as dementia where the majority of resources in geriatric mental health are allocated. Perhaps this stigma may prevent individuals from acknowledging their mental illness and thus accessing available services. There is even evidence to suggest that physicians themselves may contribute to this stigma by holding negative attitudes and stereotypes of older adults with schizophrenia [42].

One possible solution to combating social isolation would be to allocate funds towards intervention programs, such as home or telephone visits, which have been shown to be effective in community-dwelling seniors [43]. With regards to the stigma of mental health in the elderly, awareness and education are important first steps to normalizing the issue, which can be achieved through educating oneself, one's colleagues, one's medical trainees (both residents and medical students), and one's elderly patients by engaging in open and frank discussions [44,45]. These efforts, along with expanding research and services to include older adults may ensure better care for these patients.

Conclusion

Older adults with first-onset schizophrenia have historically been overlooked. This paper discussed three main barriers that have contributed to the lack of understanding, under-recognition and under-service of this patient population. Difficulties with inconsistent terminology and definitions over the years, diagnostic challenges, as well as limited services, treatment, and research for this patient group constitute these barriers. Terminology can become more standardized by conducting field studies on older-onset schizophrenia patients and subsequently incorporating the different subsets into diagnostic manuals. In addition, incorporating (V) LOS into the learning objectives for medical learners would allow this terminology to be more widely recognized. The obstacles to obtaining a diagnosis can be overcome by establishing clear diagnostic guidelines for these patients. Finally, more services for early intervention, with opportunities for patients to participate in research studies, as well as targeted efforts to help these patients and healthcare providers overcome the stigma of mental health would all be beneficial.

As the population ages, the number of patients with LOS and especially VLOS is expected to significantly increase. Therefore, recognizing these illnesses and properly caring for such patients will be an essential skill for every clinician who works with adult patients. Substantial education, research, and innovative ideas are required in order to overcome the barriers discussed above, and more analyses are needed to identify others. With these efforts, healthcare providers can ultimately provide better service to this vulnerable patient population.

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