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Schizophrenia: A Disease

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OPINION

Over the last century, the understanding of schizophrenia as a disease entity has evolved significantly. Kraepelin distinguished chronic psychoses from functional deterioration (dementia praecox) and episodic psychoses (manic-depressive insanity). The subsequent literature revealed significant clinical overlap between these diseases leading to the diagnosis of schizoaffective disorder which is fairly defined and thus unreliable. These categories have mostly remained the same during the last century as reflected in the current classification systems the Diagnostic and Statistical Manual of Mental Disorders (DSM) and the International Classification of Diseases (ICD). The release of the fifth version of the DSM in 2013 was a significant recent milestone in psychiatry. Although no fundamental revisions to the criteria of schizophrenia and other psychotic diseases were made to make diagnoses more straightforward. Due to a lack of evidence supporting the validity of these divisions the Kraepelinian subtyping of schizophrenia into paranoid, disorganized, catatonic, and undifferentiated types was abolished. Second, catatonia was changed from a schizophrenia subtype to a specifier across illnesses. Finally, a more long-term approach to this diagnosis was established. Finally, the earlier focus on Schneider's first-rank symptoms (delusions of thought broadcast and thought insertion), as well as odd delusions, was dropped. Even though all of this made the criteria easier to employ the validity of the boundaries remained substantially in doubt. Over the last two decades, it has been increasingly obvious that many illnesses have neurobiological, genetic and treatment response commonalities, calling into question their legitimacy. The study domain criteria were recently introduced as a result of a dimensional approach to psychopathology and the belief that biological impairments can cut across categories. Research Domain Criteria (RDoC) is an agnostic to symptom-based diagnosis paradigm for representing accumulating information across the molecular, cellular, circuit, and behavioral domains. Although this method is currently in its early stages, it may provide a valuable framework for future research that leads to a neuroscience-based classification system. The current consideration of cognitive decline as a basic component of schizophrenia with psychosis seen by some as a later development has sparked interest in defining schizophrenia beyond the symptoms listed in the DSM. Along these lines, the concept of schizophrenia prodrome has been used to help better understand and describe schizophrenia at an earlier stage of the condition. Schizophrenia prodrome, also known as ultra-high-risk condition or psychosis risk syndrome, is a set of attenuated positive and negative symptoms that people may experience several years to months before developing schizophrenia. Early cognitive impairment is one of the risk factors for conversion to psychosis, according to research (inattention, concentration difficulties). Even though not all risk variables are identified, roughly 35% of people with prodromal symptoms develop schizophrenia. A large multi-center study called the North American Prodromal Longitudinal Study has begun to show significant neuroanatomical, neurophysiological, neurocognitive, and neuro-hormonal alterations during the prodromal phase that may contribute to the risk of schizophrenia. Since the advent of chlorpromazine, antipsychotic medicines have been the mainstay of schizophrenia treatment, concentrating on reducing the frequency and intensity of psychotic episodes while also enhancing the functional capacity of people with schizophrenia. However, because of the negative side effects and poor outcomes associated with First-Generation Antipsychotics (FGAs), Second-Generation Antipsychotics (SGAs) were developed, which are generally linked with fewer Extrapyramidal Symptoms (EPSs) than FGAs due to their 5HT-2A antagonism. However, there is disagreement regarding how FGAs and SGAs should be classified; some studies categorize them based on their potential to generate EPSs while others categorize them based on their antagonistic effects on dopamine D-2

receptors. Clozapine, the first and most effective SGA for treating refractory schizophrenia is limited by the danger of agranulocytosis which demands regular blood cell counts. Clozapine has the lowest EPS and haloperidol has the highest. Except for haloperidol, ziprasidone, and lurasidone, all other medicines cause weight gain, with olanzapine and clozapine causing the most. Risperidone and paliperidone cause the most prolactin rise. All medicines are much more sedating than placebo, except amisulpride, paliperidone, sertindole, and iloperidone. Several large-scale studies have found no obvious advantage of SGAs over FGAs in terms of positive, cognitive, or social outcomes in first-episode or chronic patients. FGAs and SGAs do not adequately target negative symptoms with only olanzapine and asenapine showing modest efficacy while they may treat positive symptoms insufficiently. Clozapine appears to be the most effective medication but the efficacy of olanzapine and risperidone in comparison to other antipsychotics is still debated. SGAs have a minor advantage over FGAs in terms of preventing recurrence. Newer antipsychotics such as asenapine, iloperidone, lurasidone, and paliperidone do not appear to be considerably better than haloperidol, while clozapine has been demonstrated to be significantly more successful than other drugs in the treatment of resistant schizophrenia. Several studies however suggest that olanzapine and risperidone are more effective than other antipsychotics but this is still debatable, and more study is needed in this area. Furthermore, amisulpride, olanzapine, clozapine, paliperidone, and risperidone have lower all-cause discontinuation than several other agents. Strong empirical support for both FGAs and SGAs in acute and maintenance therapy of schizophrenia as well as for the use of clozapine for treatment-resistant positive symptoms, aggression, and suicidal tendencies, was summarised by the Schizophrenia Patient Outcome Research Team (PORT).