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Schizophrenia Treatment and Biomarkers

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Schizophrenia is a severe chronic mental health disorder manifested with an array of symptoms, which are categorized as positive and negative with underlying impaired cognitive ability. Due to inherent heterogeneity, schizophrenia still lacks consensus on the diagnosis, etiology, and pathophysiology. While the etiology of schizophrenia has yet to be elucidated, the theories of pathophysiology mainly center on the abnormalities in neurotransmission, either an excess or a deficiency of neurotransmitters, including dopamine, serotonin, and glutamate. Other theories implicate aspartate, glycine, and gamma-aminobutyric acid (GABA) as part of the neurochemical imbalance of schizophrenia.

Patients with schizophrenia have mostly relied on a long-term medication of antipsychotics managing symptoms. The typical antipsychotic drugs (e.g., chlorpromazine and haloperidol), which is also known dopamine antagonist, neuroleptics, or the first-generation antipsychotics according to their affinity, efficacy, or in comparison with the newer drugs, reduce dopaminergic neurotransmission by blocking dopamine type 2 (D2) receptors in the dopamine pathways, which include:

1) The mesocortical pathway, in which its dysfunction may be associated with cognitive impairments and disturbances of emotions and affect (negative symptoms). The first-generation antipsychotics acting on this pathway can induce secondary negative symptoms and cognitive effects;
2) The mesolimbic pathway, in which antipsychotic effects can be involved in the pathophysiology of positive symptoms of schizophrenia;
3) the nigrostriatal pathway. Antagonism of D2 receptors in this pathway is associated with an increased risk of extrapyramidal symptoms; and
4) the tuberoinfundibular pathway, hyperprolactinemia, in which dopamine acting as a prolactin-inhibiting factor can raise prolactin levels by promoting its release in the pituitary gland. The first-generation antipsychotic drugs cause significant movement disorders such as severe muscle stiffness or tardive dyskinesia.

In the recent two decades, atypical drugs became available, which include clozapine, olanzapine, risperidone, quetiapine, and ziprasidone. The clinical study has shown that the second-generation medicines are more effective, especially olanzapine and risperidone in treating patients with chronic schizophrenia, they tend to produce fewer extrapyramidal side effect and to manage more negative symptoms of schizophrenia, but adverse effects such as

weight gain, hyperglycemia, hyper- or dyslipidemia, and hyperprolactinemia are relatively common.

Recently, psychotherapy such as CBT alone in patients with schizophrenia seems a feasible and safe treatment compared with the standard antipsychotics or combination (Morrison, Law, et al. 2018); although this was based on a study with a small sample size. Psychotherapy may include 1) individual psychotherapy, which can teach the person how to deal with their thoughts and behaviors, 2) cognitive behavior therapy (CBT), which can help the person change their thinking and behavior, and 3) cognitive enhancement therapy (CET), which is cognitive remediation. When psychotherapy shows improvement in patients with schizophrenia, further psychosocial treatment can help them learn how to become part of a community. This includes social skills training, rehabilitation, Family education, self-help groups, coordinated specialty care (CSC), assertive community treatment (ACT), and social recovery therapy.

However, the mechanisms of all these alternative treatments are not clear; and there is still a lack of objective markers to evaluate the efficacy of individual treatment. Also, for antipsychotic medication, there is still a need to identify biomarkers that could predict the effectiveness or adverse effect and guide the precision medication. With the imaging tools and molecular techniques, the treatment-based study is promising in identifying biomarkers that could be translated into the practice of clinical psychiatry.

For the special issue, we welcome original research article, systematic review, a new concept for schizophrenia treatment including pharmacological and non-pharmacological medications, including efficacy, side-effect, and treatment study that include molecular study. The full manuscript can be submitted online https://www.gcatresearch.com/manuscript-submission/first-submission/.