

# Unraveling the Mechanisms of Schizophrenia

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Schizophrenia, which currently affects around one percent of the American population, is possibly one of the most puzzling mental health disorders. Essentially, it is a complex biochemical brain disorder that affects the way that you perceive and interact with the world around you. It can affect anyone, and does not have a cure. Schizophrenia is clinically characterized by positive and negative symptoms, as well as cognitive deficits, in particular, domains related to attention and verbal working memory. Currently, treatment involves antipsychotic medication to combat symptoms, including hallucinations, delusions, disorganized speech etc., as well as counselling to help with problems-solving and taking control of daily activities.

Since the 1950's, research efforts on understanding the pathophysiology of schizophrenia were dominated by the theory that too much of the dopamine neurotransmitter caused the disorder. Although many symptoms can be explained by an increase in dopamine, recent research has suggested that the cause of the disorder may be lie somewhere else. Specifically, GABA, a primary inhibitory neurotransmitter in the brain, has been increasingly recognized as having a significant role in the pathophysiology of the disorder. Post-mortem studies of schizophrenia have shown a decreased expression of a key enzyme in the biosynthesis of GABA. However, studies examining the relationship between GABA and schizophrenia, involving living patients, have been inconclusive.

The Karolinska Schizophrenia Project is a relatively new project that brings together researchers from different scientific backgrounds to build a more thorough understanding of the disorder and discover new options for drug therapy. They have published two studies, both in the journal, *Molecular Psychiatry*, with the most recent paper examining cerebral spinal fluid (CSF) concentrations of GABA in patients who have experienced their first episode of psychosis (FEP).

The Measurement and Treatment Research to Improve Cognition (MATRICS) in Schizophrenia Consensus Cognitive Battery, contains a series of cognitive tests used to determine the speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition, in each individual participating in the clinical study. After the cognitive tests were performed, concentrations of GABA in the patient's cerebrospinal fluid were analyzed through brain scans, and results were compared to healthy individuals of the same age and gender, who had also taken the cognitive test. Interestingly, researchers found that FEP patients showed a reduction in cerebrospinal fluid GABA concentrations compared to healthy individuals, and along with these thought-provoking results, they discovered that GABA concentrations were negatively correlated with symptom levels, meaning that lower GABA concentrations

predicted higher symptom levels, and therefore a high general severity of the illness.

Many comparative studies with animals have shown this same relationship between GABA concentrations and schizophrenia, but this study is the first to clinically demonstrate the GABA hypothesis in living humans. The novel results of this paper have paved the way for continued research, not only in studying schizophrenia, but with other similar psychotic disorders. Goran Engberg, and other contributors to the Karolinska Project, stated that "to the best of our knowledge, the present study is the first to show that first episode psychosis patients show low cerebrospinal fluid GABA levels and that this condition is associated with the severity of the illness, psychotic symptoms, and probably attentional deficits." The researchers of the Karolinska Schizophrenia Project have mentioned follow-up studies examining the potential causes of this difference in GABA concentrations, because it remains unclear as to whether they are a result, or a cause of the disorder. The goal of this research project and many research projects like it, is to better understand the biological mechanisms of schizophrenia, in hopes of finding new and more effective ways to treat individuals suffering from this disorder.

## FURTHER READING

F Orhan, H Fatouros-Bergman, M Goiny, A Malmqvist, F Piehl, Göran Engberg, Sophie Erhardt, Lilly Schwieler, Funda Orhan, Anna Malmqvist, Mikael Hedberg, Lars Farde, Simon Cervenka, Lena Flyckt, Karin Collste, Pauliina Ikonen, Fredrik Piehl, Ingrid Agartz, S Cervenka, K Collste, P Victorsson, C M Sellgren, L Flyckt, S Erhardt, G Engberg. *CSF GABA is reduced in first-episode psychosis and associates to symptom severity*. *Molecular Psychiatry*, 2017; DOI: 10.1038/MP.2017.25

<https://www.sciencedaily.com/releases/2017/03/170314081539.htm>

<http://www.matricsinc.org/>

[http://www.cmha.ca/mental\\_health/facts-about-schizophrenia/#.WNglK-BlrKu5](http://www.cmha.ca/mental_health/facts-about-schizophrenia/#.WNglK-BlrKu5) <http://ki.se/en/startpage>