

# Incorrectly cleaved protein leads to schizophrenia

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Schizophrenia is a disease that strikes an average of 4000 Belgians every year. The causes of this psychiatric disorder are not yet clear. But now, VIB researchers connected to the Katholieke Universiteit Leuven have discovered that a disturbed cleavage of the Nrg-1 protein lies at the basis of the development of the disease. Greater understanding of this molecular process is a first step toward improved diagnosis and more effective treatment of schizophrenia and other related disorders.

Schizophrenia is a mental disorder that appears in about 1 out of every 250 Belgians, manifesting most often between the ages of 15 and 30. This disease of the brain seriously disturbs the person's thinking, emotional life, and behavior. The disease is characterized by episodes of psychotic symptoms: abnormal ideas and changes in perception, behavior and thinking occur, through which it is difficult to understand how the person feels. Typical symptoms of the disorder are: delusions, hallucinations, chaotic behavior, etc.

Up to now, no clear cause of schizophrenia has been found, although hereditary factors certainly play a role in the development of the disease. In addition, living and working conditions determine the disorder's progress. Research into schizophrenia has also shown that there is a disturbance of the activity of the frontal and temporal areas in the brain, which is connected with a disturbed equilibrium among the substances (proteins) that are needed for neuronal functioning. Schizophrenia is treated using anti-psychotic and neuroleptic medicines.

The molecular story hidden behind schizophrenia is still not at all clear. However, previous scientific studies have indeed shown that a disturbed functioning of the Nrg-1 protein is linked to the development of the disease. Now, the recent research results obtained by Tim Dejaegere and his colleagues connected to VIB and K.U.Leuven reveal how the functioning of Nrg-1 becomes disturbed.

The Nrg-1 protein – an essential factor in the development and proper functioning of our nervous system and, consequently, in the functioning of our brain – can carry out its function properly only after it has been cleaved in the right way. This cleavage is the responsibility of a molecular 'scissors' called Aph1B/C-gamma-secretase. When this scissors is absent, Nrg-1 is not cleaved, which leads to behavioral disturbances in laboratory animals that bear a striking similarity to some of the symptoms of schizophrenia. This syndrome can be corrected by administering anti-psychotic medicines. Additional studies have also shown that a genetic alteration near the site of Nrg-1 cleavage, which was detected in schizophrenia patients and which increases the risk of this disease, results in incorrect cleavage of Nrg-1 by the gamma-secretase.

The researchers are suggesting that a disturbed cleavage of Nrg-1 plays a crucial role in the development of schizophrenia and other related psychiatric disorders. This discovery is a new step forward in the quest for improved diagnosis and targeted treatment of the disease.

Source: VIB (the Flanders Institute for Biotechnology)

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